UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE, Plaintiff, v. IMSTEM BIOTECHNOLOGY, INC., XIAOFANG WANG, and REN-HE XU, Defendants.	C.A. NO. 1:17-cv-12239-ADB

ASTELLAS' TRIAL BRIEF

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Pursuant to Local Rule 16.5(f) and the Court's Amended Scheduling Order and Pretrial Order (Dkt. 106), Plaintiff Astellas Institute for Regenerative Medicine ("Plaintiff" or "Astellas") submits this Trial Brief.

I. INVENTORSHIP

A. Astellas' Proposed Findings of Fact on Inventorship

1. The Court already ruled on summary judgment that Astellas had proven by clear and convincing evidence that Drs. Kimbrel and Lanza are at least co-inventors on U.S. Patent No. 9,745,551 ("the '551 patent"), which Defendants filed naming only Drs. Wang and Xu as inventors without informing Astellas.

2. Astellas seeks to have Drs. Wang and Xu removed as inventors on the '551 patent because they did not make any significant, inventive contribution to the '551 patent's claims.

3. Defendants assert that Dr. Wang should be added as a co-inventor on Astellas' U.S. Patent No. 8,961,956 ("the '956 patent") and that Drs. Wang and Xu should be added as co-inventors on Astellas' U.S. Patent No. 8,962,321 ("the '321 patent").

4. Below, Astellas breaks out its proposed findings of fact and requested rulings of law on a patent-by-patent basis.

1. U.S. Patent No. 9,745,551 ("The '551 Patent")

5. The '551 patent claims a method of generating mesenchymal stem cells ("MSCs") from human embryonic stem cells ("hESCs") via an hemangioblast ("HB") intermediate and the cells that are created by that method ("HB-MSCs"). (Ex. A, AIRM00290341-411 at -410, '551 patent at claims.)

6. The '551 patent currently only lists Defendants Xiaofang Wang and Ren-He Xu as inventors and Defendant ImStem as the assignee on the face of the patent. (*Id.* at AIRM00290342.)

7. As this Court held on summary judgment, Astellas proved by clear and convincing evidence that "Drs. Kimbrel and Lanza provided [Drs. Wang and Xu] with the protocol to generate HB-MSCs," a point that Defendants did not contest. (Dkt. 163 at 7-9.)

8. This Court also found that Defendants "have no factual basis to dispute" that Drs. Kimbrel and Lanza "made a significant contribution to the invention." (*Id.* at 8.) The Court found that Drs. Kimbrel and Lanza are at least co-inventors to the '551 patent. (*Id.* at 9.)

9. Unlike Drs. Kimbrel and Lanza, Drs. Wang and Xu are not co-inventors on the '551 patent. Drs. Wang and Xu did not make any significant contribution to the '551 patent, as would be required to be a co-inventor.

10. Defendants initially alleged[1] that Drs. Wang and Xu contributed to the first step—and only to the first step—of the method of making HB-MSCs that is recited in Claim 1 of the '551 patent, the only independent claim. (Ex. V, Resp. to Interrog. No. 1 at pp. 5-6, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at pp. 5-6, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).) Defendants also alleged that they contributed the specific GSK3 inhibitor, BIO, to dependent claim 11. (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. US, Resp. to Interrog. No. 1 at pp. 7-8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

[1] After Astellas served its opening expert reports on inventorship of the '551 patent relying on Defendants' sworn initial interrogatory responses, Defendants served "amended" interrogatory responses drastically changing their positions, by alleging that they made the following additional contributions to the '551 patent's claims: screening HB-MSCs for low IL-6 expression (claims 1 & 2), and irradiating (or mitotically inactivating) the HB-MSCs (claims 6 & 7). (*See* Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 9-12, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) For the reasons discussed *infra* with respect to the '551 patent and to Astellas' '321 and '956 patents, these belatedly alleged contributions are not a basis for Drs. Wang and/or Xu to be co-inventors on any of these patents.

11. As to the remaining claims of the '551 patent, Defendants admitted that "[t]he remaining dependent claims recite additional useful, but not independently inventive features. *Id.* These features, while not separately patentable, provide claims that are patentable, because as dependent claims, they automatically include the novel and inventive concepts of step (a)." (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at pp. 7-8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

12. Defendants also admitted that Dr. Kimbrel carried out the remaining four steps in claim 1 of the '551 patent prior to Defendants' alleged invention. (Ex. V, Resp. to Interrog. No. 1 at p. 5, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at p. 5, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019); *see also* Dkt. 163 at 3 (undisputed that "Dr. Kimbrel provided Drs. Wang and Xu with her confidential protocol for making hemangioblasts from human embryonic stem cells, and for making HB-MSCs.").)

13. Thus, Defendants originally alleged that Drs. Wang and Xu contributed a total of four things to the claims of the '551 patent. These consist of "four parts" to the first step of Claim 1 of the '551 patent (from which the remaining claims depend): "(1) culturing real (not MA-09) hESCs, (2) doing so in a serum-free media, (3) doing so in the absence of feeder cells, and (4) doing so in the presence of inhibitors of GSK3, at 0.1 [sic[2]] to 0.2 µM," and specifically the GSK3 inhibitor called "BIO" or (2'Z,3'E)-6-Bromoindirubin-3'oxime (dependent claim 11). (Ex. V, Resp. to Interrog. No. 1 at pp. 5-6 & 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas'

[2] Claim 1 recites "at least one GSK3 inhibitor at a concentration ranging from ***0.05µM*** to 0.2 µM." (Ex. A, AIRM00290341-411 at -410, '551 patent at claim 1 (emphasis added).)

First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at pp. 5-6 & 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

14. The earliest possible date for assessing the state of the art for the inventorship analysis for the '551 patent is in the June 2010 timeframe, when Defendants allege that Drs. Wang and Xu first became aware of Astellas' HB-MSCs. (*See* Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 6-7, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).)

15. As explained below, step (a) of claim 1 of the '551 patent merely recites a well-known technique for culturing hESCs to maintain them in an undifferentiated, or pluripotent, state.

a. Culturing hESCs in the presence of GSK3 inhibitors, and specifically the GSK3 inhibitor BIO, in a concentration range of 0.05 µM to 0.2 µM, was known in the art

16. In 2004, Dr. Ali Brivanlou and his colleagues published a method of culturing hESCs to maintain them in an undifferentiated state by including a GSK3 inhibitor, specifically BIO, in the culture media. (Ex. 7, AIRM00289996-90004 at AIRM00289999-90002 Sato, N., et. al., (2004) Maintenance of Pluripotency in Human and Mouse Embryonic Stem Cells through Activation of Wnt Signaling by a Pharmacological GSK-3-Specific Inhibitor, *Nature Medicine*, 10(1):55-63 at 58-61.) Dr. Brivanlou reported that hESCs cultured in the presence of a GSK3 inhibitor, specifically BIO, maintained their pluripotency without feeder cells or conditioned media. (*Id.*)

17. In 2006, Dr. Brivanlou's group published a protocol further teaching scientists how to culture hESCs using the GSK3 inhibitor BIO without feeder cells or conditioned media. (Ex. 34, AIRM00290005-018 Sato, N. & Brivanlou, A.H., (2006) Manipulation of Self-Renewal in Human Embryonic Stem Cells Through a Novel Pharmacological GSK-3 Inhibitor, in HUMAN EMBRYONIC STEM CELL PROTOCOLS, 115-128 at 116-17, 119-21 (Humana Press).)

18. While Dr. Brivanlou reported that the typical concentration range of the GSK3 inhibitor BIO that worked with their hESC lines was 1 to 5 μM, the protocol instructed that "[t]he optimal concentration of the GSK-3 inhibitor (BIO) should be predetermined for each hESCs line by testing different concentration of BIO." (*Id.* at 125-26.) Dr. Brivanlou further taught that using the minimal effective concentration of BIO to maintain hESCs was "critical" in order to avoid hESC death or negative effects on hESC growth rate. (*Id.*)

19. Dr. Brivanlou's 2006 published protocol taught scientists to start at a relatively low concentration of BIO (1 to 5 μM), but to optimize that concentration downward to the lowest effective amount. (*Id.*)

20. Dr. Brivanlou and his colleagues also filed a patent application on their method of culturing hESCs by adding the GSK3 inhibitor BIO in culture media without feeder cells to maintain the hESCs in an undifferentiated, pluripotent state. (Ex. 33, AIRM00298309-354, U.S. Patent App. Pub. No. US2009/0111177 at abstract.) Published in 2009, Dr. Brivanlou's patent application disclosed that "[e]ffective concentrations of 6-bromoindirubin-3'oxime [BIO] in the culture medium for maintaining the undifferentiated state are about 0.001 μM to about 100 μM, ***preferably about 0.1 to about 10 μM*** and ***most preferably 1μM.***" (*Id.* at ¶ [0040] (emphasis added).)

21. More than a year before the earliest date Drs. Wang and Xu allege they began their GSK3 inhibitor work, Dr. Brivanlou taught that use of 0.05 μM to 0.2 μM of a GSK3 inhibitor in feeder-free culture effectively maintains hESCs in an undifferentiated state as recited in step (a) of claim 1 of the '551 patent. (Ex. 33, AIRM00298309-354 U.S. Patent App. Pub. No. US2009/0111177 at ¶ [0040]; Ex. 34, AIRM00290005-018 Sato, N. & Brivanlou, A.H., (2006) Manipulation of Self-Renewal in Human Embryonic Stem Cells Through a Novel

Pharmacological GSK-3 Inhibitor, in HUMAN EMBRYONIC STEM CELL PROTOCOLS, 115-128 at 116-17, 119-21 (Humana Press); Ex. 7, AIRM00289996-90004 at AIRM00289999-90002 Sato, N., et. al., (2004) Maintenance of Pluripotency in Human and Mouse Embryonic Stem Cells through Activation of Wnt Signaling by a Pharmacological GSK-3-Specific Inhibitor, *Nature Medicine*, 10(1):55-63 at 58-61.)

22. Defendants' internal documents show that Drs. Wang and Xu recognized that Dr. Brivanlou already knew of and had reported culturing hESCs with a GSK3 inhibitor at low concentration ranges to maintain those hESCs in an undifferentiated state. Dr. Wang sent Dr. Xu an internal presentation on February 28, 2011, where Dr. Wang cited Dr. Brivanlou's 2004 paper for the proposition that "Bio(2μM) has been shown to maintain hESC culture in CM for 5 days(Ali H Brivanlou, Nature Medicine 2004)." (Ex. W, IMSTEM-0008154-155 at -155.)

23. Dr. Wang removed reference to Dr. Brivanlou's 2004 paper in later versions of this presentation. In an April 5, 2011 draft, Dr. Wang deleted the above quoted bullet point, replacing it with "[w]e found another small molecular(X1) can maintain hES culture for up to 12 passages without change pluripotency." (Ex. X, IMSTEM-0011499 at slide 18 ("Using small molecular(X1) to improve mTeSR1 culture").) In 2017, Dr. Wang submitted selected, edited slides from a similar presentation to the U.S. Patent and Trademark Office ("USPTO") accompanying his declaration swearing that his invention in the '551 patent happened before the priority date of Astellas' HB-MSC patent applications. (Ex. 8, AIRM00293495-5992 at -5784-85, -788-89.) There, Dr. Wang deleted the reference to Dr. Brivanlou's 2004 article and instead represented to the USPTO that "[w]e found another small molecular(BIO) [sic] can maintain hES culture for up to 12 passages without change pluripotency." (*Id.* at AIRM00295789.)

b. Culturing hESCs in the absence of feeder cells ("feeder-free") was known in the art

24. Unless treated with certain proteins, cytokines, or chemicals, hESCs will grow and change ("differentiate") into different cell types. (*See* Dkt. 199-22 at p. 28, Brivanlou Rpt. ¶ 70; Ex. GN, AIRM00289941-947 at AIRM00289943, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42.)

25. Scientists have long known that hESCs can be kept in their undifferentiated (or "pluripotent") state if the hESCs are cultured in the presence of certain signaling molecules. (*See* Dkt. 199-22 at pp. 28-29, Brivanlou Rpt. ¶ 71; Ex. GN, AIRM00289941-947 at AIRM00289943, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42.) These signaling molecules can come from different sources. (*Id.*)

26. One known source of these signaling molecules was "feeder cells" that are typically mouse embryonic fibroblasts ("MEFs"), although human embryonic feeder cells have also been used. (*See* Dkt. 199-22 at pp. 28-29, Brivanlou Rpt. ¶ 71; Ex. GN, AIRM00289941-947 at AIRM00289943, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42.)

27. Scientists reported, by at least 2004, that the signaling molecules produced by feeder cells were used with hESCs in two ways. In the first method, feeder cells were cultured in the same dish as the hESC cells. (Ex. GN, AIRM00289941-947 at AIRM00289943, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42; *See* Dkt. 199-22 at pp. 28-29, Brivanlou Rpt. ¶ 71.) In the second method, feeder cells were cultured separately, then the media into which the feeder cells released the signaling molecules was collected, pooled, and filtered ("conditioned media"). Scientists then

added this conditioned media to hESCs. (Ex. GN, AIRM00289941-947 at AIRM00289944-45, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42; *see* Dkt. 199-22 at p. 29, Brivanlou Rpt. ¶ 72.) This second method, using conditioned media, is a "feeder-free" method. (Ex. GN, AIRM00289941-947 at AIRM00289944-45, Xu, C. & Carpenter, M.K. (2004) Feeder-Free Culture in HANDBOOK OF STEM CELLS VOL. 1 EMBRYONIC (Lanza, R., et al. eds.) 535-42; *see* Dkt. 199-22 at p. 29, Brivanlou Rpt. ¶ 72.)

28. Scientists also reported, by at least 2004, that synthetic chemicals could be used as signaling molecules to maintain hESCs in an undifferentiated state. (Ex. 7, AIRM00289996-90004 at AIRM00289993 Sato, N., et. al., (2004) Maintenance of Pluripotency in Human and Mouse Embryonic Stem Cells through Activation of Wnt Signaling by a Pharmacological GSK-3-Specific Inhibitor, *Nature Medicine*, 10(1):55-63 at 58-61; *see* Dkt. 199-22 at pp. 31-32, Brivanlou Rpt. ¶ 75-76.) Dr. Brivanlou's 2004 article reports that the GSK-3 inhibitor, BIO, is one such synthetic compound that "might therefore be useful for standardizing the quality of HESCs, rather than the undefined, feeder cell-derived factor(s) used in the current culture protocol." (Ex. 7, AIRM00289996-90004 at AIRM00289993 Sato, N., et. al., (2004) Maintenance of Pluripotency in Human and Mouse Embryonic Stem Cells through Activation of Wnt Signaling by a Pharmacological GSK-3-Specific Inhibitor, *Nature Medicine*, 10(1):55-63 at 58-61.)

29. In 2005, Dr. Lanza and his colleagues reported another system that "allows cell-free and serum-free derivation of new embryonic stem-cell lines." (Ex. GP, AIRM00290132-139 at AIRM00290136, Klimanskaya, I., Chung, Y., Meisner, L., Johnson, J., West, M.D., & Lanza, R. (2005) Human embryonic stem cells derived without feeder cells. *Lancet*. 365:1636-41.) They

reported that this "system also allowed robust and reliable maintenance of established human embryonic stem cells in feeder-layer-free and serum-free conditions." (*Id.*)

30. Dr. Lanza and Lu also reported in their patent [3] on methods of making hemangioblasts ("HBs") from hESCs and the resulting HBs, that the hESCs used in their method could be cultured "in any way known in the art, such as in the presence or absence of feeder cells." (Ex. 41, AIRM00296310-387 at AIRM00296350 (21:32-35) Lanza, R. & Lu, S.J. U.S. Patent No. 8,017,393, Hemangio-colony forming cells (published as U.S. 2008/0014180 A1 on Jan. 17, 2008, issued Sept. 13, 2011).) This application that issued as this patent published on January 17, 2008. (*Id.* at AIRM00296310 ("Prior Publication Data").)

c. Culturing hESCs without serum in the media ("serum-free") was known in the art

31. In 2005, Dr. Lanza and his colleagues reported another system that "allows cell-free and serum-free derivation of new embryonic stem-cell lines." (Ex. GP, AIRM00290132-139 at AIRM00290136, Klimanskaya, I., Chung, Y., Meisner, L., Johnson, J., West, M.D., & Lanza, R. (2005) Human embryonic stem cells derived without feeder cells. *Lancet*. 365:1636-41.) They reported that this "system also allowed robust and reliable maintenance of established human embryonic stem cells in feeder-layer-free and serum-free conditions." (*Id.*)

32. Dr. Lanza and Lu also reported in their patent on methods of making hemangioblasts ("HBs") from hESCs and the resulting HBs, that their "invention provides methods of generating and expanding human hemangioblasts from embryonic stem cells in which no serum is used." (Ex. 41, AIRM00296310-387 at AIRM00296350 (21:36-61) Lanza, R. & Lu,

[3] The disclosure of this patent was incorporated by reference in Astellas' '321 and '956 patents and thus became part of the HB-MSC method disclosed therein. (Ex. 1, AIRM00293424-494 '321 patent at 19:51-60; Ex. 2, AIRM00290412-497 '956 patent at 21:44-53.)

S.J. U.S. Patent No. 8,017,393, Hemangio-colony forming cells (published as U.S. 2008/0014180 A1 on Jan. 17, 2008, issued Sept. 13, 2011).) It further reports that "serum-free media is used throughout the method of this invention" and that "[i]n the first step of this method for generating and expanding human hemangioblast cells, human stem cells are grown in serum-free media." (*Id.*) This application that issued as this patent published on January 17, 2008. (*Id.* at AIRM00296310 ("Prior Publication Data").)

33. Dr. Lanza and his colleagues also reported culturing hESCs in serum-free media in their 2007 article in *Nature Methods*. (Ex. 6, AIRM00289971-979, at AIRM00289971, Lu, S.J., Feng, Q., Caballero, S., Chen, Y., Moore, M.A.S., Grant, M.B., & Lanza, R. (2007) Generation of functional hemangioblasts from human embryonic stem cells. *Nature Methods.* 4:501-09.) Specifically, they reported that "we generated early-stage embryoid bodies (EBs) from hES cells (WA01 (H1)-GFP+) cultured in serum-free medium." (*Id.*)

34. Dr. Wang described Dr. Lanza's 2007 *Nature Methods* article as a "serum free, defined system" in his April 5, 2011 departmental presentation. (Ex. X, IMSTEM-0011499 at slides 13-14; Wang Dep. Tr. at 123:11-18.)

d. The MA09 hESC line is a "real" hESC line

35. Defendants appear to have dropped this allegation, as they removed it from their amended responses to Astellas' interrogatory. Defendants served these amended responses after Astellas' experts pointed out in their opening reports that the MA09 hESC line meets the express definition of hESCs in the '551 patent and that the '551 patent specifically identifies the MA09 line as an hESC line from which its claimed HB-MSCs were and may be made. (*See* Ex. FB, Amend. Resp. to Interrog. No. 1 at p. 6, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019); *see See* Dkt. 199-22 at pp. 137-41, Brivanlou Rpt. ¶¶ 246-256.) Astellas provides these proposed findings of fact in the event that Defendants try to resurrect this issue.

36. The ’551 patent identifies the MA09 cell line as “an FDA approved, clinical grade cell line derived at Advanced Cell Technology, Inc. (Klimanskaya et al (2006))” (Ex. A, AIRM00290341-441 at -402, ’551 patent 51:2-8), and includes data from experiments where HB-MSCs made from the MA09 cell line were used (*see, e.g., id.* at Figs. 5A-C, 6A-F, 12-A-C, 16A-B, 25; *see also* Wang Dep. Tr. 77:11-16 (“Q. All right. So the MSCs from Astellas, based on the MA09 cell line, were used as an example in the patent to show it would work? [. . .] A. Yes.”).)

e. The ’551 patent indicates that the significant invention is Astellas’ HB-MSC method and resulting cells, not Defendants’ alleged contributions

37. Throughout, the ’551 patent’s specification indicates that the significant invention described in the patent is Astellas’ HB-MSC method and the resulting cells from that method.

38. The Introduction of the ’551 patent states that the “present invention relates to a method of generating mesenchymal stem cells from human embryonic stem cells using a multi-step method.” (Ex. A, AIRM00290341-441 at -377, ’551 patent 1:20-30.) This multi-step method involves culturing hESCs, culturing the hESCs in conditions to differentiate them into embryoid bodies (“EBs”), culturing the EBs in conditions to differentiate them into HBs (called “hemangio-colony forming cells”), and culturing the HBs to differentiate them into MSCs. (*Id.*)

39. The description of the invention in the Introduction does not specify that 1) the disclosed method must use a glycogen synthase kinase-3 (“GSK3”) inhibitor in a particular amount, 2) that the hESCs must be cultured feeder-free, or 3) that the hESCs must be cultured in serum-free media. (*See* Dkt. 199-22 at p. 116, Brivanlou Rpt. ¶ 113.)

40. The “Background” section of the ’551 patent describes how Astellas’ invention, (*i.e.*, making HB-MSCs and the resulting cells) solves the problem with prior art methods:

> It has been reported that human embryonic stem cells (hESC) can differentiate into embryoid bodies (EB), and then into a pool of cells with hemangioblast (HB) activities, i.e. they can further differentiate

> into vascular smooth muscle cells, endothelial cells, and hematopoietic cells (Chyou et al. (2008); Lu et al. (2007); Lu et al. (2009)). Therefore it was reasoned that a portion of these HB-containing cells could differentiate into MSCs, thus, eliminating the problems found with bone marrow-derived MSCs. These mesenchymal stem cells derived from human embryonic stem cell would be an unlimited, safe, and consistent supply of stem cells to be used to treat and prevent autoimmune diseases.

(Ex. A, AIRM00290341-411 at AIRM00290377 '551 patent at 2:63-3:5.)

41. This Background section description does not relate the asserted benefits of the claimed invention (*i.e.*, an "unlimited, safe, and consistent supply of stem cells to be used to treat and prevent autoimmune diseases") to 1) use of a glycogen synthase kinase-3 ("GSK3") inhibitor in a particular amount, 2) culturing hESCs feeder-free, or 3) culturing hESCs in serum-free media. (*See id.*) Instead, this section relates the asserted benefits of the claimed invention to Astellas' method—deriving MSCs from hESCs via an HB intermediate.

42. The "Summary of the Invention" section of the '551 patent describes Astellas' invention. It states that the "invention is based on the surprising discovery that a portion of the HB-containing cells derived from embryonic stem cells (hES), can also differentiate into MSC, designated 'hES-MSC', with high efficiency and consistency." (Ex. A, AIRM00290341-411 at AIRM00290377 '551 patent at 3:13-46; *see also id.* at 2:65 (defining "HB" as "hemangioblast").)

43. This initial summary of the invention does not mention 1) use of a glycogen synthase kinase-3 ("GSK3") inhibitor in a particular amount, 2) culturing hESCs feeder-free, or 3) culturing hESCs in serum-free media. (*See id.*) Instead, this section relates the asserted benefits of the claimed invention to Astellas' method—deriving MSCs from hESCs via an HB intermediate.

44. The entire Summary of the Invention, which spans almost five columns of text, does not mention 1) use of a glycogen synthase kinase-3 ("GSK3") inhibitor in a particular amount,

or 2) culturing hESCs feeder-free. (*See* Ex. A, AIRM00290341-411 at AIRM00290377-380, '551 patent at 3:13-8:3.)

45. The entire Summary of the Invention includes a single embodiment of the invention that involves culturing cells in serum-free medium. (*See* Ex. A, AIRM00290341-411 at AIRM00290377-380 '551 patent at 3:47-67.) But it also indicates that serum-containing media may be used, stating "[i]n certain embodiments, the serum-containing medium contains fetal calf serum, L-glutamine and the serum-free medium contains knockout serum replacement (KOSR) or bovine serum albumin (BSA)." (*Id.* at AIRM002903780-380 '551 patent at 4:14-17.)

46. The '551 patent's specification, which contains 68 columns of text, mentions use of a GSK3 inhibitor in the descriptive text in only four places out of 68 columns of text (*see id.* at AIRM00290381, -383, & -402, '551 patent at 10:28-37, 13:47-54, 51:8-14, & 52:9-18) and in only three of thirty-one figures (*compare id.* at AIRM00290373-375, *with id.* at AIRM00290346-372, & -376).

47. One mention of use of a glycogen synthase kinase-3 ("GSK3") inhibitor in the narrative text of the '551 patent indicates that using a GSK3 inhibitor at the hESC culture step is merely one optional way to culture hESCs:

> The human embryonic stem cells or induced pluripotent stem cell may be the starting material of this method. The embryonic stem cells or iPS may be cultured in any way known in the art, such as in the presence or absence of feeder cells. Adding GSK3 inhibitor BIO at 0.05 μM-0.2 μM can increase the embryoid body formation and subsequent hemangioblast forming efficiency, shortening the culture time.

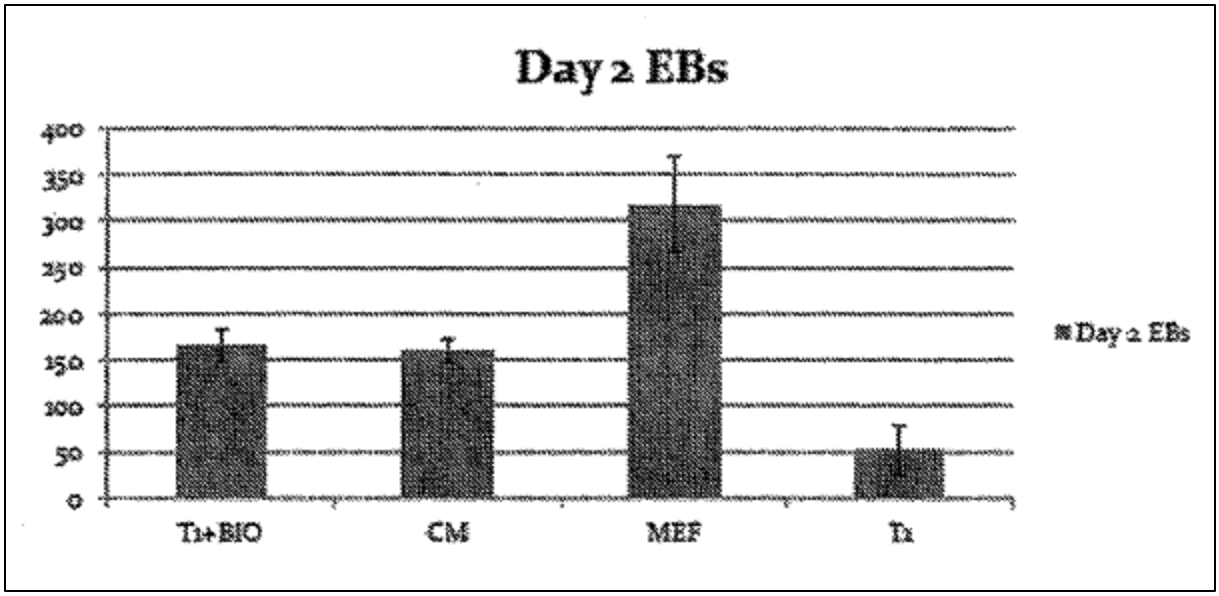
(*Id.* at AIRM00290383 '551 patent at 13:47-54.) This reference to a GSK3 inhibitor expressly acknowledges that feeder-free culture was known in the art, that the purpose of the first step in the process of claim 1 was merely to culture hESCs, and that any purported benefit from adding a GSK3 inhibitor was in the formation of hemangioblasts, shortening the culture time.

48. A second mention of use of a glycogen synthase kinase-3 ("GSK3") inhibitor in the narrative text of the '551 patent explicitly states that its use is optional. In describing the hESC cell lines used in certain experiments described in the '551 patent, it states that these cell lines were cultured in different ways, including "in TeSR1 medium (Stem Cell Technologies, Vancouver, Canada), with or without adding of 0.05-0.2 µM of BIO (6-Bromoindirubin-3'-oxime (CAS 667463-62-9))." (*Id*. at AIRM00290402 '551 patent at 51:8-14.) The '551 patent does not suggest that the resulting MSCs had any improved properties when cultured with versus without a GSK3 inhibitor.

49. The remaining two mentions of use of a glycogen synthase kinase-3 ("GSK3") inhibitor in the text of the '551 patent simply describe the data in Figures 28, 29, and 30. (Ex. A, AIRM00290341-411 at AIRM00290381 '551 patent at 10:28-37 (Brief Description of the Drawings section); *id.* at AIRM00290402 '551 patent at 52:9-18 (describing data in Figs. 28, 29, and 30 as reporting "EB and HB formation efficiency").)

50. Figures 28, 29, and 30 of the '551 patent do not concern the effects of treatment of hESCs with a GSK3 inhibitor on MSCs. (Ex. A, AIRM00290341-411 at AIRM00290381 '551 patent at 10:28-37.) Rather, these figures only show data for effects "on the differentiation of embryoid bodies (EB) from hES cells" (Fig. 28), on "EB formation numbers" (Fig. 29), or "hemangioblast forming efficiency" (Fig. 30). (*Id.*)

51. Figure 29 shows that hESCs cultured with the GSK3 inhibitor BIO produced about the same or fewer EBs as hESCs cultured using conditioned medium ("CM") or on feeder cells ("MEF"), respectively:



(Ex. A, AIRM00290341-411 at AIRM00290374 '551 patent at Fig. 29.) This figure also shows that all three treatments (GSK3 inhibitor BIO, conditioned medium, and feeder cells) produced more EBs than culturing hESCs in a commercially available mTesr1 Medium ("T1"). (*Id.* at AIRM00290381 '551 patent at 10:28-37.)

52. Figures 28, 29, and 30 do not report data showing the effect of MSCs that were made by a method involving treatment of hESCs with a GSK3 inhibitor in the Experimental Autoimmune Encephalomyelitis ("EAE") animal model of multiple sclerosis.

53. The '551 patent includes results of MSCs made from various hESC lines, including MA09 and CT2. Astellas never provided MA09 hESCs to Drs. Wang and Xu. The HB-MSCs made from MA09 hESCs discussed in the '551 patent were made at Astellas without the use of a GSK3 inhibitor. (Wang Dep. Tr. 196:4-16.)

54. The '551 patent does not report that HB-MSCs have different properties when cultured in the presence versus the absence of a GSK3 inhibitor. The data in the '551 patent shows the exact opposite—that HB-MSCs made with or without use of a GSK3 inhibitor at the hESC culturing step have similar efficacy in an animal model of multiple sclerosis. (Ex. A at Figs. 5A-

C, 6A-F, 12-A-C, 16A-B, 25 (reporting data from HB-MSCs made from the MA09 hESC line); Wang Dep. Tr. 196:4-197:6 (Astellas provided HB-MSCs made from MA09 line and Dr. Wang does not know if a GSK3 inhibitor was used when making them); Wang Dep. Tr. at 77:11-14, 77:15 (agreeing that "MSCs from Astellas, based on the MA09 cell line, were used as an example in the patent to show it would work").)

55. In total, the '551 patent teaches that use of a GSK3 inhibitor is not a significant part of the invention claimed in the patent. Rather, the patent reports and the figures show that it is an optional additive that has no effect on the qualities of the HB-MSCs or their therapeutic efficacy.

f. The prosecution history of '551 patent does not indicate that Defendants' alleged contributions are "significant"

56. The prosecution history of the '551 patent likewise indicates that none of Drs. Wang and/or Xu's alleged contributions are significant to the claimed invention.

57. The '551 patent claims priority to two provisional applications: U.S. Provisional Application No. 61/670,787 ("the '787 provisional") and U.S. Provisional Application No. 61/762,961 ("the '961 provisional").

58. Defendants Wang and Xu filed the '787 provisional on July 12, 2012. (Ex. 3, AIRM00296616-646 at AIRM00296644 '787 provisional at filing receipt.)

59. There is no discussion or reference to using a GSK3 inhibitor or BIO in the method of making MSCs described in the '787 provisional, as the attorney who prosecuted the '551 patent admitted. (*See generally* Ex. 3, AIRM00296616-646 at AIRM00296627 '787 provisional; Cheng Dep. Tr. 74:24-77:2.)

60. Defendants Wang and Xu filed the '961 provisional on February 11, 2013. (Ex. 5, AIRM00296647-675 at AIRM00296673, '961 provisional at filing receipt.)

61. The ’961 provisional discloses “methods to obtain MSC-like cells from human embryonic stem cells so called [sic] hES-HB-MSCs , hES-T-MSCs or hES-MSCs” in its Abstract. (Ex. 5, AIRM00296647-675 at AIRM00296656, ’961 provisional at abstract.) The claims of this provisional patent recite a method of making MSCs with immunosuppressive characteristics, methods of determining the immunosuppressive activity level of those cells, and genetically modifying adult-tissue derived MSCs to change certain properties of those cells. (Ex. 5, AIRM00296616-646 at AIRM00296624-29, ’961 provisional at claims.)

62. There is no discussion or reference to using a GSK3 inhibitor or BIO in the method of making MSCs described in the ’961 provisional. (*See generally* Ex. 5, AIRM00296616-646 at AIRM00296624-29, ’961 provisional.)

63. The ’961 provisional discloses culturing hESCs using “mouse embryonic fibroblast (MEF) as feeders.” (Ex. 5, AIRM00296647-675 at AIRM00296664, ’961 provisional at Material and Method.)

64. Defendants admitted in their summary judgment briefing that it was Defendants’ PCT/US2013/048291, filed on June 27, 2013, that disclosed the GSK3 inhibitor step “for the first time in any patent application.” (Dkt. 152 at 4.)

65. Defendants’ originally filed claims in the application that issued as the ’551 patent specifically recited that the first step of culturing hESCs could be accomplished “with or without GSK3 inhibitors.” (Ex. 40, AIRM00293495-5992 at -646-49, File History at 2015.01.07 Claims; Zerhusen Dep. Tr. 56:7-57:9 (admitting that “the defendants’ initial claim had the GSK inhibitor step as an optional step”).)

66. Defendants only amended their claims to require use of a specified amount of a GSK3 inhibitor ***after*** the USPTO rejected their claims as “anticipated by,” or claiming the exact

same ***invention*** as, Astellas' HB-MSC PCT application. (Ex. 40, AIRM00293495-5992 at -495, File History at 2016.07.28 Rejection at 5-6 ("In the instant case, Lanza teaches the same method steps to produce the same cells."); *id*. at AIRM00295774-96, File History at 2017.01.17 Amendment.) Defendants filed this amendment on January 17, 2017. (*Id.*)

67. In connection with their Amendment, Drs. Wang and Xu submitted a sworn declaration "swearing behind the priority date and publication date of Lanza" and therefore arguing that Lanza did not constitute prior art. (Ex. 40, AIRM00293495-5992 at -784-86, File History at 2017.01.17 Amendment at Ex. A Declaration.) As the Court found on summary judgment, "Defendants thus clearly stated, under oath, that the '321 patent was not prior art." (Dkt. 163 at 8.)

68. In their January 17, 2017 amendment filing, Defendants did not disclose to the USPTO that they had collaborated with Astellas scientists regarding Astellas' HB-MSCs, or that they had received Astellas' protocol for making HB-MSCs from Astellas as part of this collaboration.

69. In their January 17, 2017 sworn declaration and Amendment, Drs. Wang and Xu also concealed from the USPTO that they were aware of a scientific article, published over five years before Defendants' alleged conception, that reported use of a GSK3 inhibitor, specifically BIO, to maintain hESCs in culture in an undifferentiated state. As part of the "[r]ecords evidencing [Defendants'] possession" of the alleged invention prior to Astellas' HB-MSC patent applications, Drs. Wang and Xu submitted some selected, edited slides from an internal presentation. (Ex. 40, AIRM00293495-5992 at -784-86, File History at 2017.01.17 Amendment at Ex. A Declaration.) One of these submitted slides states "[w]e found another small molecular(BIO) [sic] can maintain hES culture for up to 12 passages without change pluripotency" and identifies BIO as "a GSK3

inhibitor." (*Id.* at AIRM00295789.) In contrast, a similar slide from a similar presentation Dr. Wang sent Dr. Xu on February 18, 2011 attributes the discovery that the GSK3 inhibitor BIO can maintain hESCs undifferentiated (*i.e.*, maintain their pluripotency) in culture to Dr. Brivanlou. (Ex. W, IMSTEM-0008154-155 at -155 ("Bio(2μM) has been shown to maintain hESC culture in CM for 5 days(Ali H Brivanlou, Nature Medicine 2004")).

70. While the patent examiner concluded, after Defendants submitted their sworn declaration and edited records, that the GSK3 inhibitor limitation "overcomes the rejections of record" (Ex. 40, AIRM00293495-5992 at AIRM00295959), the examiner did not consider Dr. Brivanlou's later publications (i.e., his 2006 and 2009 publications discussed *infra*) that expanded upon the teachings of his 2004 paper, and expressly taught use of the GSK3 inhibitor BIO at lower concentrations, as claimed in the '551 patent. (*See* Ex. A, AIRM00290341-411 at -342-45, '551 patent at item (56) References Cited; *see also* Zerhusen Dep. Tr. 54:24-55:10 (Defendants' patent attorney expert admitting that he was not aware "whether the examiner had in front of him the Brivanlou 2006 or 2009 papers dealing with GSK-3").)

g. None of the remaining claim elements of the '551 patent are "significant"

71. In March 2019, before expert discovery, Defendants admitted that all the remaining limitations of the '551 patent's claims (*i.e.*, everything other than the four alleged inventive contributions in step (a) of claim 1 discussed *supra*) were not "independently inventive" features sufficient to warrant co-inventorship. Specifically, Defendants' admitted that "[t]he remaining dependent claims recite useful, but not independently inventive features," and that "while not separately patentable," their inventiveness depends solely on the four alleged "inventive concepts" in step (a) of claim 1. (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's

Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

72. After fact witness depositions were complete and Astellas' experts relied on Defendants' admission in their reports on the correct inventorship of the '551 patent, Defendants reversed course, amending their admissions to state that certain of these previously "not independently inventive features" are, in fact, inventive and that Drs. Wang and Xu invented them. Specifically, Defendants newly alleged that Dr. Wang and Xu contributed the notion of screening HB-MSCs for low IL-6 expression as recited in claims 1 and 2 of the '551 patent, and an additional step of mitotically inactivating the MSCs by irradiation as recited in claims 6 and 7 of the '551 patent. (Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 9-10, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) Defendants did not allege in these amended responses that Drs. Wang or Xu contributed the idea of comparing a property of HB-MSCs with that of BM-MSCs as recited in claim 5 of the '551 patent. (*See id.* at pp. 5-13; Ex. A '551 patent at claim 5.) Nonetheless, for the reasons discussed *infra* with respect to Defendants' allegations of co-inventorship on Astellas' patents in Sections I.A.1, I.A.2, and I.B.2 (¶¶ 73 - 148, 173 - 188) these alleged contributions do not warrant co-inventorship for Drs. Wang and Xu on any patent-in-suit.

2. U.S. Patent No. 8,961,956 ("The '956 Patent") and U.S. Patent No. 8,962,321 ("The '321 Patent")

73. Plaintiff Astellas is the successor in interest to Advanced Cell Technology, Inc., Ocata Therapeutics, Inc., and Stem Cell & Regenerative Medicine International, Inc. ("SCRMI").

74. Plaintiff Astellas is the owner and assignee of U.S. Patent No. 8,962,321 ("the '321 patent"). (Ex GA, AIRM00297774-80; Attach. A to Pretrial Memo. at Stip. Fact No. 3.)

75. The ’321 patent issued on February 24, 2015, is titled “Mesenchymal Stromal Cells And Uses Related Thereto,” and lists Erin Anne Kimbrel, Robert Lanza, Jianlin Chu, and Nicholas Arthur Kouris as inventors.[4] (Ex. 1, AIRM00293424-494 at -425; Attach. A to Pretrial Memo. at Stip. Fact No. 4.) The application that issued as the ’321 patent was filed on November 30, 2012. (Attach. A to Pretrial Memo. at Stip. Fact No. 5.) The ’321 patent claims priority to U.S. Provisional Application No. 61/565,358, which was filed on November 30, 2011. (Attach. A to Pretrial Memo. at Stip. Fact No. 6.) The application that issued as the ’321 patent was published as U.S. Patent Application Publication No. US2013/0183272 on July 18, 2013. (Attach. A to Pretrial Memo. at Stip. Fact No. 7.)

76. Plaintiff Astellas is the owner and current assignee of U.S. Patent No. 8,961,956 (“the ’956 patent”). (Ex. GA, AIRM00297774-80; Attach. A to Pretrial Memo. at Stip. Fact No. 8.)

77. The ’956 patent issued on February 24, 2015, is titled “Mesenchymal Stromal Cells And Uses Related Thereto,” and lists Erin Anne Kimbrel, Robert Lanza, Jianlin Chu, and Nicholas Arthur Kouris as inventors. (Ex. 2, AIRM00290412-97 at -413; Attach. A to Pretrial Memo. at Stip. Fact No. 9.) The application that issued as the ’956 patent was filed on May 30, 2013, as a continuation-in-part of the application that issued as U.S. Patent No. 8,962,321. (Attach. A to Pretrial Memo. at Stip. Fact No. 10.) The ’956 patent claims priority to U.S. Provisional Application No. 61/565,358, which was filed on November 30, 2011. (Attach. A to Pretrial Memo. at Stip. Fact No. 11.) The application that issued as the ’956 patent was published as U.S. Patent

[4] Dr. Chu’s and Dr. Kouris’s contributions to the claims of the Astellas patents are not at issue in this case.

Application Publication No. US2014/0072537 on March 13, 2014. (Attach. A to Pretrial Memo. at Stip. Fact No. 12.)

78. Plaintiff Astellas is the owner of U.S. Provisional Application No. 61/565,358 ("the '358 provisional"). (Attach. A to Pretrial Memo. at Stip. Fact No. 14.) The '358 provisional was filed on November 30, 2011. (*See* Ex. 35 at filing receipt; Attach. A to Pretrial Memo. at Stip. Fact No. 14.)

79. Plaintiff Astellas is the owner of PCT Application No. PCT/US2012/0067464, which was filed on November 30, 2012 and published as WO2013/082543 on June 6, 2013. (*See* Ex. P, AIRM00294150-299 at -150; Attach. A to Pretrial Memo. at Stip. Fact No. 15.)

80. PCT Application No. PCT/US2012/0067464 claims priority to the '358 provisional. (*See* Ex. P, AIRM00294150-299 at -150; Attach. A to Pretrial Memo. at Stip. Fact No. 16.)

81. The '956 patent generally claims a method of treating diseases and disorders using MSCs derived from hESCs through an HB intermediate. (Ex. 2, AIRM00290412-97 at -496-97, '956 patent at claims.)

82. The '321 patent claims a method of generating MSCs from hESCs via an HB intermediary and the HB-MSCs generated by the method. (Ex. 1, AIRM00293424-494 at -492-93, '321 patent at claims.)

83. Defendants seek to add Dr. Wang as a co-inventor of the '956 patent.[5] (Dkt. 91 at ¶¶ 34-48.)

[5] The Court denied Defendants' motion to amend to add a counterclaim that Dr. Xu is a co-inventor of the '956 patent. (Dkt. 85 at 10-11.) Thus, only Defendants' claim that Dr. Wang should be a co-inventor on the '956 patent will be addressed at trial.

84. Defendants seek to add Drs. Wang and Xu as co-inventors of the '321 patent.[6] (Dkt. 91 at ¶¶ 34-48.)

b. Dr. Wang did not conceive of suggesting that MSCs could be used to treat multiple sclerosis or other autoimmune diseases

85. Defendants allege that, before and during a meeting with Dr. Lu from Astellas in Massachusetts on July 13, 2010, Drs. Wang and Xu conceived of using HB-MSCs to treat multiple sclerosis and other autoimmune diseases as recited in claims 3 and 4 of the '956 patent. (Ex. FB, (Amend. Resp. to Interrog. No. 1 at pp. 6-8, No. 8 at p. 23, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).)

86. In January 2018, Defendants alleged that Dr. Wang alone, and not Dr. Xu, came up with this idea. (*See* Dkt. 20 at 12, ¶ 2 ("At the outset of the collaboration, Dr. Wang suggested that the parties study MSC's functionality in treating autoimmune disorders, including multiple sclerosis.").) It was not until over a year and a half later that Defendants changed their position to allege that both Drs. Wang and Xu made this suggestion. (*See* Dkt. 91 at 12, ¶ 2; *see also* Dkt. 71-2 at 13, ¶ 2 (edit to add Dr. Xu in redline).)

87. Defendants proffer no evidence other than Drs. Wang and Xu's testimony that they first had the idea of testing Astellas' HB-MSCs in the mouse EAE model for autoimmune diseases around this July 13, 2010 meeting.

88. Defendants' expert, Dr. Bunnell, has only opined that Drs. Wang and Xu "are ***likely*** the source of the invention of using HB-MSCs for the treatment of MS and autoimmune diseases because they were experts in that field, and the features they added to the '321 and '956 patents

[6] Defendants' own counsel admitted in March 2018 that Dr. Wang "had nothing to do with the 321 patent concerning the generation of the cells." (Ex. EY, LU-00000003-090 at -069-70 (67:18-68:3).)

are consistent with a deep understanding of the science and therapeutic context." (*See* Dkt. 199-24 at p. 11, Bunnell Open. Rpt. ¶ 65 (emphasis added).)

89. As evident from Astellas' contemporaneous internal emails and documents, before ever meeting with Defendants, Astellas' scientists began their work to develop HB-MSCs with the goal of making cells that could modulate the immune system and that could be used therapeutically to treat numerous diseases, including autoimmune diseases like multiple sclerosis. Dr. Lanza had been following an extensive literature on preclinical and clinical studies of MSCs for therapeutic purposes, including using MSCs for treating autoimmune diseases.

90. In September 2009, Dr. Lanza forwarded an article on MSCs made by another company to an Astellas scientist and asked whether the Astellas team could make "ESC-derived cells with similar characteristics/immunomodulatory properties." (Ex. 38, AIRM00223725-731 at -725).) The attached article specifically identified that MSCs could be used to treat "Multiple sclerosis" and "Immunological disorders." (Ex. EZ, AIRM00013304-310 at -308).) That Astellas scientist, in turn, forwarded that email to Dr. Kimbrel and other Astellas scientists, explaining that Dr. Lanza was "really interested" in seeing if they could make MSCs through a hemangioblast intermediate. (*Id.* at -304).)

91. Dr. Kimbrel, whose project at Astellas focused on making immunotherapeutic cells, was tasked with figuring out how to make HB-MSCs. Her work during this time and leading up to the first interactions with Drs. Wang and Xu is evident in her various lab meeting presentations, her laboratory notebook, and scientific progress reports. (*See*, *e.g.*, Ex. 36, AIRM00281690-713; Ex. 45, AIRM00290141-340 at -245; Ex. 44, AIRM00200724-730; Ex. IA, AIRM00281769-791.)

92. In late 2009 to early 2010, Dr. Kimbrel, in consultation with Dr. Lanza, successfully developed the method of differentiating MSCs from hemangioblasts. (Ex. 45, AIRM00290141-340.)

93. After spending considerable time experimenting with culturing and characterizing the immunological properties of HB-MSCs, by May 2010, Dr. Kimbrel had produced 17 million HB-MSCs for her project on the "use of hemangioblasts for production of immunotherapeutic cells." (Ex. IA, AIRM00281769-791 at AIRM00281777, -778.) This was in contrast to her production of 4 million MSCs using the previously known "direct differentiation" method. (*Id.*)

94. Prior to beginning their collaboration with Drs. Wang and Xu, Astellas scientists had developed the HB-MSC method, the HB-MSCs themselves, and the use of HB-MSCs to treat the diseases and disorders as disclosed in the Astellas patents. (*See, e.g.*, Dkt. 163 at 3 (finding that Drs. Kimbrel and Lanza developed the method for making HB-MSCs and Dr. Kimbrel provided her confidential protocol for making HB-MSCs to Drs. Wang and Xu).)

95. Once Astellas had the method for making HB-MSCs and the resulting cells, Astellas began looking for collaborators who could verify that Astellas' HB-MSCs had the expected therapeutic efficacy of MSCs in various animal models. (Lanza Dep. 106:23-107:5 (confirming that when Astellas successfully made HB-MSCs, Dr. Lanza "consider[ed] it an obvious next step to try them in animal models").)

96. At the time of the collaboration, Astellas did not have its own animal facility. (Kimbrel Dep. 223:15-225:1.)

97. There is no evidence that Dr. Wang (or Dr. Xu) had any expertise or ever actually worked on MSCs before receiving Astellas' HB-MSCs during collaboration. (*See* Wang Dep. 282:23-285:4; Ex. BT, IMSTEM-0042945-3138 at -945-61, May 2010-August 2010 lab notebook

entries showing no work with MSCs; Ex. CD, IMSTEM-0042855, Dec. 2009 discussing MSCs as potential product for business with no actual work.)

98. When Dr. Wang first started culturing Astellas' HB-MSCs, Dr. Kimbrel had to look over his shoulder and teach him how to carry out Astellas' derivation protocol. (Kimbrel Dep. 240:7-23.)

99. There is no evidence that Dr. Wang (or Dr. Xu) had any expertise in clinical application of MSCs or use of animal models for testing MSCs for clinical therapy. (*See, e.g.*, Xu Dep. 43:6-8 (admitting that he had not done any research into multiple sclerosis or any autoimmune disease prior to Dr. Wang joining his lab as a postdoc), 43:11-18 (had no publications on EAE)); Ex. 24, IMSTEM-0003560 (Dr. Xu's lab was not cleared for EAE animal testing until June 2011); Wang Dep. 66:9-16 (Dr. Wang's prior knowledge was limited to TH17 response in multiple sclerosis in his thesis).)

100. Defendants offer a book chapter that Dr. Wang wrote with Dr. Xu in Spring 2010 as including their idea of using hESC-derived MSCs in treating autoimmune diseases such as multiple sclerosis. (Ex. FB, Amend. Resp. to Interrog. No. 1 at p. 6, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) This book chapter does not reflect any actual experience or research from Dr. Wang or Xu. It is a review of the state of the art at the time it was written. (Ex. BZ, IMSTEM-0042283-383.) The only reference to multiple sclerosis in the two pages in the chapter about MSCs cites to work published by others in 2004. (Ex. FD, AIRM00297929-958 at -947).

101. On July 29, 2010, Dr. Kimbrel wrote to Dr. Wang "in regards to Shi-Jiang Lu's email about a potential collaboration." Dr. Kimbrel explained that "[c]urrently, I have several vials of hemangioblast-derived 'MSCs' frozen down." (Ex. 11, IMSTEM-0001523-30 at

IMSTEM-0001526.) Dr. Kimbrel also requested Dr. Wang send her relevant papers on the EAE mouse model. (*Id.*)

102. On August 3, 2010, Dr. Wang replied. Dr. Wang wrote that "[t]here are many labs have found some mechanism of how MSC suppresses immuno [sic] function" and that "[t]here are some reviews out there" with a citation to one such review. (Ex. 11, IMSTEM-0001523-30 at IMSTEM-0001525.) Dr. Wang also wrote that "[s]ome report that hESC-MSC have stronger immunosuppressive activity than BM derived MSC, and some report show MSC can be introduced into mice for disease model. Both mouse and human MSC have been used to ameliorate EAE(an autoimmune disease)" followed by links to several published papers. (*Id.*) Dr. Wang also stated that he could test Astellas' HB-MSCs in the EAE model "pretty easily." (*Id.*)

103. Dr. Wang did not personally perform the first test of Astellas' HB-MSCs in the EAE model. Rather, he took Astellas' HB-MSCs to his former colleagues at Yale, and these Yale scientists performed the test. (Ex. AC, IMSTEM-0002267-268; Wang Dep. 188:22-24 (stating that he "brought the cells to Yale and someone else performed the experiments").)

104. When Dr. Wang finally performed EAE tests using Astellas' HB-MSCs, he used a commercial kit that Astellas purchased for him from Hooke Labs. (Ex. LL, IMSTEM-0008839; Ex. GT, IMSTEM-0005455-457; Ex. A, AIRM00290341-411 at -403, '551 patent at 53:12-19 (using "EAE Induction Kit (Hooke Laboratories, Inc., Mass. (Cat. #EK- 0114)) following the manufacturer's protocol").)

105. As Dr. Wang explained, using the Hooke Labs kits was something any scientist could do because Hooke Labs "do everything for you . . . only thing you need to [sic] is inject the mice." (Ex. 15, IMSTEM-0008426-427; Ex. 74, AIRM00299372-378.)

106. Defendants' own emails and grant application, the '551 patent, and the Parties' co-authored 2014 Stem Cell Reports paper all recognized that the EAE model was a well-known mouse model and had been commonly used to test MSCs in the past. (Ex. W, IMSTEM-0008154-155; Ex. MF, IMSTEM-0040175-207; Ex. A, AIRM00290341-411 at -377, '551 patent at 2:26-29, 2:29-38; Ex. 9, AIRM00289980-995 at -980.)

107. Numerous articles, published before Dr. Wang ever met with Astellas scientists in 2010, reported tests of MSCs in the EAE mouse model. (*See, e.g.*, Ex. HU, Zhang, J., Li, Y., Chen, J., Cui, Y., Lu, M., Elias, S.B., Mitchell, J.B., Hammill, L., Vanguri, P., & Chopp, M. (2005) Human bone marrow stromal cell treatment improves neurological functional recovery in EAE mice. *Experimental Neurology*. 195:16-26; Ex. 60, Zappia, E., Casazza, S., Pedemonte, E., Benvenuto, F., Bonanni, I., Gerdoni, E., Giunti, D., Ceravolo, A., Cazzanti, F., Frassoni, F., Mancardi, G., & Uccelli, A. (2005) Mesenchymal stem cells ameliorate experimental autoimmune encephalomyelitis inducing T-cell anergy. *Blood*. 106(5):1755-1761; Ex. HE, Gerdoni, E., Gallow, B., Casazza, S., Musio, S., Bonanni, I., Pedemonte, E., Mantegazza, R., Frassoni, F., Mancardi, G., Pedotti, R., Uccelli, A. (2007) Mesenchymal stem cells effectively modulate pathogenic immune response in experimental autoimmune encephalomyelitis. *Annals of Neurology*. 61:219-227; Ex. HJ, Kassis, I., Grigoriadis, N., Gowda-Kurkalli, B., Mizrachi-Kol, R., Ben-Hur, T., Slavin, S., Abramsky, O., & Karussis, D. (2008) Neuroprotection and immunomodulation with mesenchymal stem cells in chronic experimental autoimmune encephalomyelitis. *Archives of Neurology*. 65(6):753-761; Ex. 58, Gordon, D., Pavlovska, G., Glover, C.P., Uney, J.B., Wraith, D., & Scolding, N.J. (2008) Human mesenchymal stem cells abrogate experimental allergic encephalomyelitis after intraperitoneal injection, and with sparse CNS infiltration. *Neuroscience Letters*. 448(1):71-73.)

108. Other articles, also published before Dr. Wang ever met with Astellas scientists in 2010, discussed use of MSCs in clinical trials as promising therapeutics for multiple sclerosis. (*See, e.g.*, Ex. HL, Mohyeddin Bonab, M., Yazdanbakhsh, S., Alimoghaddom, K., Ghavamzadeh, A., Hooshmand, F., Lotfi, J., Talebian, F., & Nikbin, B. (2005) Mesenchymal stem cell therapy for multiple sclerosis. *International J. of Hematology, Oncology and Bone Marrow Transplantation*. 2(5):10-14; Ex. HM, Mohyeddin Bonab, M., Yazdanbakhsh, S., Lotfi, J., Alimoghaddom, K., Talebian, F., Hooshmand, F., Ghavamzadeh, A., & Nikbin, B. (2007) Does mesenchymal stem cell therapy help multiple sclerosis patients? Report of a pilot study. *Iranian J. of Immunology*. 4(1):50-57; Ex. HI, Karussis, D. & Kassis, I. (2008) The potential use of stem cells in multiple sclerosis: an overview of the preclinical experience. *Clinical Neurology and Neurosurgery*. 110:889-896; Ex. HS, Slavin, S., Kurkalli, B.G.S., & Karussis, D. (2008) The potential use of adult stem cells for the treatment of multiple sclerosis and other neurodegenerative disorders. *Clinical Neurology and Neurosurgery*. 110:943-946; Ex. HK, Liang, J. Zhang, H., Hua, B., Wang, H., Wang, J., Han, Z., & Sun, L. (2009) Allogeneic mesenchymal stem cells transplantation in treatment of multiple sclerosis. *Multiple Sclerosis*. 15:644-646.)

109. Testing Astellas' HB-MSCs in the EAE model was nothing novel, given that hESC-derived MSCs had been shown to have similar immunoproperties to adult-derived MSCs. (*See, e.g.*, Ex. GR, AIRM00171102-111; Ex. 59, AIRM00299528-537; Ex. HT, AIRM00299584-593.)

110. Besides the EAE data, the '956 patent includes results from other collaborators' testing of Astellas' HB-MSCs in standard animal models for autoimmune diseases. (Ex. 2, AIRM00290412-97, '956 patent at 83:50-84:9 (Example 23 "Lupus Model"), 65:1-66:32 (Example 20 "Pain Study"), 66:34-67:50 (Example 21 "Uveitis Study").) The potency shown in the animal models only verified the therapeutic efficacy of Astellas' HB-MSCs.

c. Dr. Wang did not conceive of suggesting to investigate the amount of IL-6 expression by Astellas' HB-MSCs as claimed in the '956 patent

111. Defendants allege that Dr. Wang conceived of the idea of screening HB-MSCs for low IL-6 expression as recited in claim 9 of the '956 patent. (Ex. FB, Amend. Resp. to Interrog. No. 8 at p. 23, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).)

112. Defendants also alleged that Drs. Wang and Xu contributed to the low IL-6 expression of HB-MSCs as claimed in the '551 patent. (Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 9-12, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) However, Defendants admitted that this feature was "not independently inventive" and "not separately patentable" in their original, March 2019 responses to this same interrogatory. (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019)); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

113. According to Defendants, Dr. Wang's IL-6 investigation involved a microarray experiment. Dr. Wang did not start preparing samples for the microarray experiment, which tested over 47,000 genes, until June 2012. (Ex. FB, Amend. Resp. to Interrog. No. 1 at p. 9, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) Dr. Wang received his first microarray results on June 22, 2012. (Ex. FC, IMSTEM-0011870.) According to Defendants, Dr. Wang then confirmed these results using a flow cytometry experiment for IL-6, on August 20, 2012. (Ex. FB, Amend. Resp. to Interrog. No. 1 at p. 9, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).)

114. Dr. Kimbrel investigated IL-6 expression in HB-MSCs earlier than Dr. Wang.

115. On February 3, 2012, Dr. Kimbrel designed a custom cytokine antibody array to target 20 specific cytokines including IL-6, and on March 28, 2012, she had received data

comparing the secretion levels of these 20 cytokines from Astellas' HB-MSCs with those from BM-MSCs. (Ex. 62, AIRM00297348-369 at AIRM00297365-367; Ex. HZ, AIRM00170061; Ex. 63, AIRM00297370; Ex. 43, AIRM00051817-837 at AIRM00051817, -823 (data from "032812.conditioned.medium.raybio.custom.blots.ppt").)

116. In April 2012, Dr. Kimbrel presented her results in a lab meeting that showed that IL-6 expression was substantially lower in HB-MSCs than in BM-MSCs. (Ex. 62, AIRM00297348-369 at AIRM00297365-367); *see also* Ex. 43, AIRM00051817-837 at AIRM00051817, -823 (data from "032812.conditioned.medium.raybio.custom.blots.ppt").)

117. Dr. Kimbrel's IL-6 data is incorporated in the '956 and '321 patents as FIGs. 30-31. (Ex. 62, AIRM00297348-369 at -819, -821 & -823; Ex. 2, AIRM00290412-497 at -446-47, '956 patent at FIGs. 30-31; Ex 1, AIRM00293424-494 at -458-59, '321 patent at FIGs. 30-31.)

118. When Dr. Kimbrel shared her IL-6 data with Drs. Wang and Xu later, they included this data in their own grant application without giving credit or getting permission from Dr. Kimbrel. (Ex. FR, IMSTEM-0021416.)

119. Dr. Kimbrel's approach to investigating IL-6 expression was more targeted than Dr. Wang's microarray experiment. Dr. Kimbrel designed a custom cytokine antibody array to target 20 specific cytokines including IL-6, while Dr. Wang's later microarray experiment screened over 47,000 different genes.

120. Given that his experiment screened over 47,000 genes, Dr. Wang's later microarray experiment does not suggest that Dr. Wang had the idea to investigate IL-6 expression prior to seeing the results from his experiment in June 2012.

121. Dr. Wang's June 2012 microarray experiment showed either higher or similar expression of IL-6 in HB-MSCs as compared with BM-MSCs, opposite to what Defendants claim to be their invention. (Ex. FC, IMSTEM-0011870.)

122. Dr. Wang did not tell Dr. Kimbrel that he had tested and seen lower IL-6 expression in HB-MSCs until November 5, 2012. (Ex. 46, AIRM00023998-002.)

123. Numerous articles, published before Dr. Wang ever met with Astellas scientists in 2010, reported investigating how much IL-6 is expressed by MSCs, IL-6 levels in multiple sclerosis patients, and/or IL-6 levels in relation to EAE experiments. (Ex. HF, Haynesworth, S.E., Baber, M.A., & Caplan, A. (1996) Cytokine expression by human marrow-derived mesenchymal progenitor cells in vitro: effects of dexamethasone and IL-1α. *J. Cellular Physiology*. 166:585-592; Ex. HR, Samoilova, E.G., Horton, J.L., Hilliard, B., Liu, T.-S. T., & Chen, Y. (1998) IL-6-deficient mice are resistant to Experimental Autoimmune Encephalomyelitis: roles of IL-6 in the activation and differentiation of autoreactive T cells. *J. of Immunology*. 161:6480-6486; Ex. HW, Lock, C., Hermans, G., Pedontiti, R., et al. (2002) Gene-microarray analysis of multiple sclerosis lesions yields new targets validated in autoimmune encephalomyelitis. *Nature Medicine*. 8(5): 500-508; Ex. HH, Ishihara, K. & Hirano, T. (2002) IL-6 in autoimmune disease and chronic inflammatory proliferative disease. *Cytokine & Growth Factor Reviews*. 13: 357-368; Ex. HO, Potian, J.A., Aviv, H., Ponzio, M., Harrison, J.S., & Rameshwar, P. (2003) Veto-like activity of mesenchymal stem cells: functional discrimination between cellular responses to alloantigens and recall antigens. *J. of Immunology*. 171:3426-3434; Ex. HN, Park, C.W., Kim, K.-S., Bae, S., Son, H.K., Myung, P.-K., Hong, H.J., & Kim, H. (2009) Cytokine secretion profiling of human mesenchymal stem cells by antibody array. *International J. of Stem Cells*. 2(1):59-68; Ex. 61, Hwang, J.H., Shim, S.S., Seok, O.S., Lee, H.Y., Woo, S.K., Kim, B.H., Song, H.R., Lee, J.K.,

Park, Y.K. (2009) Comparison of cytokine expression in mesenchymal stem cells from human placenta, cord blood, and bone marrow. *J. Korean Medical Sciences*. 24:547-54.)

d. Dr. Wang did not conceive of mitotically inactivating MSCs as claimed in the '956 patent and Drs. Wang and Xu did not conceive of the same as claimed in the '321 patent

124. Defendants allege that Drs. Wang and Xu conceived of the idea of mitotically inactivating HB-MSCs as recited in claim 5 of the '956 patent and claims 17 and 18 of the '321 patent. (Ex. FB, Amend. Resp. to Interrog. No. 8 at p. 23, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019); Ex. MI, Resp. to Interrog. No. 31 at p. 6, Defs.' Amend. Obj. & Resp. to Plaintiffs' Third Set of Interrog. (Oct. 15, 2019).)

125. On August 11, 2019, the Court denied Defendants' motion to amend their counterclaims to assert a claim to add Dr. Xu as an inventor on the '956 patent. (Dkt. 85 at 11.) The Court explained:

> There is no excuse for Dr. Xu's lack of diligence in asserting counterclaims related to the '956 Patent. Dr. Xu's co-defendants, ImStem and Dr. Wang, asserted a counterclaim seeking a correction of inventorship on the '956 Patent on January 10, 2018. [ECF No. 20]. Dr. Xu did not file his own answer until June 8, 2018, at which time he had been on notice of the Counterclaim Complaint for nearly six months. [ECF No. 33]. At the time of the filing of the proposed amended counterclaims, Dr. Xu had been aware of the Counterclaim Complaint for over eighteen months. This apparent indifference by Dr. Xu cannot be overcome by any geographic or language barriers that he or his counsel may face and precludes a finding of good cause.

(*Id*.)

126. There is no evidence that Dr. Wang or Dr. Xu had any expertise or ever performed any work relating to mitotic inactivation before meeting with Astellas.

127. Drs. Wang and Xu's 2010 book chapter, a review of others' work in the field, admits that it was not their idea but common knowledge in the art that suggested to mitotically

inactivate hESC-derived MSCs before clinical trials to avoid formation of tumors. (Ex. FD, AIRM00297929-958 at -937, -947.)

128. Drs. Wang and Xu's December 2010-January 2011 grant application, which Defendants point to for a discussion of mitotic inactivation (Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 11-12, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019), disclosed nothing beyond what was already known in the field and contained Dr. Kimbrel's text and analysis. (*See* Ex. FF, AIRM00233553-572.)

129. Mitotic inactivation can be done by at least two methods: irradiating cells or by treating cells with a chemical called mitomycin C ("MMC").

130. Defendants admit that Dr. Wang did not irradiate (one method of mitotic inactivation) HB-MSCs until November 7, 2011, and did not discuss results of irradiated cells with Dr. Kimbrel until March 2012. (Ex. FB, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. at p. 12 (Oct. 15, 2019).)

131. Dr. Kimbrel had already mitotically inactivated HB-MSCs and shown that they had similar *in vitro* immunomodulatory effects to regular MSCs months before November 7, 2011. As early as August 16, 2011, Dr. Kimbrel documented her experiments mitotically inactivating MSCs by mitomycin C (another method of mitotic inactivation) in her lab notebook. (Ex. 47, AIRM00249127-323 at -238.) Dr. Kimbrel's mitotic inactivation data is incorporated in the '956 and '321 patents as Figure 10B. (Ex. 2, AIRM00290412-497 at -426, '956 patent at FIG. 10B; Ex.1, AIRM00293424-494 at -438, '321 patent at FIG. 10B.)

132. By 2009, it was well-reported in the scientific literature that cells derived from hESCs could potentially form teratomas (tumors) and that, for safety reasons, such cells should be mitotically inactivated. (*See, e.g.*, Ex. HG, Heng, B.C., Liu, H., & Cao, T. (2005) Transplanted

human embryonic stem cells as biological 'catalysts' for tissue repair and regeneration. *Medical Hypotheses*. 64:1085-1088; Ex. GZ, Fujikawa, T., Oh, S.-H., Pi, L., Hatch, H.M., Shupe, T., & Petersen, B.E. (2005) Teratoma formation leads to failure of treatment for Type I Diabetes using embryonic stem cell-derived insulin-producing cells. *American J. of Pathology*. 166(6):1781-1791; Ex. HB, Hentze, H., Graichen, R., & Colman, A. (2007) Cell therapy and the safety of embryonic stem cell-derived grafts. *Trends in Biotechnology*. 25(1):24-32; Ex. HD, Blum, B. & Benvenisty, N. (2008) The tumorigenicity of human embryonic stem cells. *Advances in Cancer Research*. 100:133-58; Ex. 56, Hentze, H., Soong, P.L., Wang, S.T., Phillips, B.W., Putti, T.C., & Dunn, N.R. (2009) Teratoma formation by human embryonic stem cells: evaluation of essential parameters for future safety studies. *Stem Cell Research*. 2:198-210.)

133. By 2009-2010, it was well-reported in the scientific literature that MSCs, including hESC-derived MSCs, had been mitotically inactivated and that the inactivated MSCs maintained their immunomodulatory properties. (*See, e.g.*, Ex. GS, Di Nicola, M., Carlo-Stella, C., Magni, M., Milanesi, M., Longoni, P.D., Matteucci, P., Grisanti, S., & Gianni, A.M. (2002) Human bone marrow stromal cells suppress T-lymphocyte proliferation induced by cellular or nonspecific mitogenic stimuli. *Blood*. 99:3838-3843; Ex. HA, Götherström, C., Ringdén, O., Westgren, M., Tammik, C., & Le Blanc, K. (2003) Immunomodulatory effects of human foetal liver-derived mesenchymal stem cells. *Bone Marrow Transplantation*. 32:265-272; Ex. HX, Le Blanc, K., Tammik, L., Sundberg, B., Haynesworth, S.E., Ringdén, O. (2003) Mesenchymal stem cells inhibit and stimulate mixed lymphocyte cultures and mitogenic responses independently of the major histocompatibility complex. *Scandinavian J. of Immunology*. 57:11-20; Ex. HQ, Rasmusson, I., Ringdén, O., Sundberg, B., & Le Blanc K. (2003) Mesenchymal stem cells inhibit the formation of cytotoxic T lymphocytes, but not activated cytotoxic T lymphocytes or natural

killer cells. *Transplantation*. 76:1208-1213; Ex. HG, Heng, B.C., Liu, H., & Cao, T. (2005) Transplanted human embryonic stem cells as biological 'catalysts' for tissue repair and regeneration. *Medical Hypotheses*. 64:1085-1088; Ex. HC, Li, C.D., Zhang, W.Y., Li, H.L., Jiang, X.X., Zhang, Y., Tang, P., & Mao, N. (2005) Mesenchymal stem cells derived from human placenta suppress allogeneic umbilical cord blood lymphocyte proliferation. *Cell Research*. 15(7):539-547; Ex. GY, Bocelli-Tyndall, C., Bracci, L., Spagnoli, G., Braccini, A., Bouchenaki, M., Ceredig, R., Pistoia, V., Martin, I., & Tyndall, A. (2007) Bone marrow mesenchymal stromal cells (BM-MSCs) from healthy donors and auto-immune disease patients reduce the proliferation of autologous- and allogeneic-stimulated lymphocytes *in vitro*. *Rheumatology*. 46:403-408; Ex. HB, Hentze, H., Graichen, R., & Colman, A. (2007) Cell therapy and the safety of embryonic stem cell-derived grafts. *Trends in Biotechnology*. 25(1):24-32; Ex. 42, Rasmusson, I., Le Blanc K., Sundberg, B., & Ringdén, O. (2007) Mesenchymal stem cells stimulate antibody secretion in human B cells. *Scandinavian J. of Immunology*. 65:336-343; Ex. HT, Tan, Z., Su, Z.-Y., Wu, R.-R., Gu, B., Liu, Y.-K., Zhao, X.-L., & Zhang, M. (2011) Immunomodulative effects of mesenchymal stem cells derived from human embryonic stem cells in vivo and in vitro. *J. Zhejiang Univ. Sci. B. (Biomed & Biotechnol)*. 12(1):18-27.)

134. Further, articles also reported that the immunomodulatory properties of these MSCs were due to MSCs secreting immunomodulatory and bioactive trophic factors. (*See, e.g.*, Ex. 31, Caplan, A.I. & Dennis, J.E. (2006) Mesenchymal stem cells as trophic mediators. *J. of Cellular Biochemistry*. 98:1076-1084.)

135. Defendants' own 2012 grant application cited numerous studies of effective inactivated MSCs." (Ex. GD, IMSTEM-0040209-281 (citing Ex. GY, AIRM00298300-305; Ex. HC, AIRM00298595-603; Ex. HA, AIRM00298556-563; Ex. HX, AIRM00299638-647).)

136. During prosecution of the ’551 patent, the patent examiner recognized that mitotic inactivation of MSCs by irradiation was known in the art. (Ex. 40, AIRM00293495-5992 at -5654 (“Lanza teaches that the MSCs can be irradiated” and “prior to the time of the claimed invention, Kato teaches irradiating MSCs using gamma irradiation”) (citing Ex. P, AIRM00294150-299 at -223, Lanza (WO2013/082543) at ¶ 278); Ex. JP, AIRM00298729-818, Canadian Patent No. 2,792,802 at 53).)

137. The ’551 patent states that irradiating HB-MSCs provides the same safety feature—protecting against teratomas—as reported in the scientific literature as a reason to mitotically inactivate hESC-derived cells:

> These data, together, suggest that irradiated hES-MSC have similar lifespan in the host mice and can achieve similar efficacy on EAE (when given at doubled dose) compared to non-irradiated hES-MSC, and ***no tumors are found in the immune-compromised mice transplanted with hES-MSC***.

(Ex. A at AIRM00290406 ’551 patent at 60:10-16 (emphasis added).)

138. Claims 7 and 8 of the ’551 patent claims cells made by the method of claim 1 that are mitotically inactivated. Despite their allegations of the purported significance of mitotic inactivation, Defendants admitted that this feature was “not independently inventive” and “not separately patentable” in their original, March 2019 interrogatory responses. (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.’ Xiaofang Wang and ImStem’s Resp. to Astellas’ First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu’s Resp. to Astellas’ First Set of Interrog. (Mar. 7, 2019).)

139. Defendants maintained this interrogatory response throughout fact discovery. Only after Astellas’ experts noted the admission in their reports did Defendants seek to amend their interrogatory response to allege that mitotic inactivation was a significant contribution in the context of the method of making HB-MSCs set forth in the ’551 patent. Defendants’ attempted

reversal as to the "inventiveness" of mitotic inactivation is not credible and is entitled to no weight in view of their prior admission.

e. Dr. Wang did not conceive of comparing HB-MSCs with BM-MSCs as claimed in the '956 patent and Drs. Wang and Xu did not conceive of the same as claimed in the '321 patent

140. Defendants alleged that in 2010, Drs. Wang and Xu conceived of the idea of comparing HB-MSCs to BM-MSCs as recited in claim 10 of the '956 patent and claim 21 of the '321 patent. (Ex. FB, Resp. to Interrog. No. 8 at p. 23, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019); Ex. MI, Resp. to Interrog. No. 31 at p. 6, Defs.' Amend. Obj. & Resp. to Plaintiffs' Third Set of Interrog. (Oct. 15, 2019).) According to Defendants, Drs. Wang and Xu memorialized this idea in a one-page draft grant proposal on December 1, 2010, and shared it with Astellas in late 2010 or January 2011. (Ex. FB, Resp. to Interrog. No. 8 at p. 23, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019) (citing Ex. AD, IMSTEM-0007426 and "IMSTEM-001788").)

141. On August 11, 2019, the Court denied Defendants' motion to amend their counterclaims to assert a claim to add Dr. Xu as an inventor on the '956 patent. (Dkt. 85 at 11.) The Court explained:

> There is no excuse for Dr. Xu's lack of diligence in asserting counterclaims related to the '956 Patent. Dr. Xu's co-defendants, ImStem and Dr. Wang, asserted a counterclaim seeking a correction of inventorship on the '956 Patent on January 10, 2018. [ECF No. 20]. Dr. Xu did not file his own answer until June 8, 2018, at which time he had been on notice of the Counterclaim Complaint for nearly six months. [ECF No. 33]. At the time of the filing of the proposed amended counterclaims, Dr. Xu had been aware of the Counterclaim Complaint for over eighteen months. This apparent indifference by Dr. Xu cannot be overcome by any geographic or language barriers that he or his counsel may face and precludes a finding of good cause.

(*Id.*)

142. As discussed *supra* ¶¶ 97 and 99, no evidence supports that Drs. Wang and Xu had expertise in the fields of multiple sclerosis, autoimmune diseases, or the immunological properties of MSCs from any source prior to the collaboration with Astellas.

143. Comparing MSCs made from a new method with MSCs from known sources, such as BM-MSCs was a typical experiment scientists would have known to perform at least as early as 2009.

144. By 2009, numerous scientific articles reported studies of BM-MSCs *in vitro*, in the EAE model, and in clinical trials. (*See, e.g.*, Ex. HU, AIRM00299602-612; Ex. HS, AIRM00299580-583.)

145. By 2009, numerous studies had reported evaluating the potency of MSCs from various sources relative to the potency of BM-MSCs. (*See, e.g.*, Ex. HV, Dicker, A., Le Blanc, K., Åström, G., van Harmelen, V., Götherström, C., Blomqvist, L., Arner, P., & Rydén, M. (2005) Functional studies of mesenchymal stem cells derived from adult human adipose tissue. *Experimental Cell Research*. 308:283-290; Ex. HP, Qiao, C., Xu, W., Zhu, W., Hu, J., Qian, H., Yin, Q., Jiang, R., Yan, Y., Mao, F., Yang, H., Wang, X., & Chen, Y. (2008) Human mesenchymal stem cells isolated from the umbilical cord. *Cell Biology International*. 32:8-15; Ex. GR, Trivedi, P. & Hematti, P. (2008) Derivation and immunological characterization of mesenchymal stromal cells from human embryonic stem cells. *Experimental Hematology*. 36:350-359.)

146. As Dr. Wang explained in his July 2010 email responding to Dr. Kimbrel, MSCs derived from hESCs using other methods had been reported to "have stronger immunosuppressive activity than BM [bone marrow] derived MSC." (Ex. 11, IMSTEM-0001523-530 at -525.)

147. Defendants admitted that the feature of comparing the amount of expression of "pro-inflammatory proteins" IFN-γR1 and IFN-γR2 by HB-MSCs and by BM-MSCs (*see* Ex. A at AIRM00290384 '551 patent at 16:50-56, claim 5) was "not independently inventive" and "not separately patentable" in their original, March 2019 interrogatory responses. (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019)); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).) Moreover, Defendants did not allege in their interrogatory responses regarding Drs. Wang and Xu's alleged contributions to the '551 patent that Drs. Wang or Xu contributed the idea of comparing a property of HB-MSCs with that of BM-MSCs as recited in claim 5 of the '551 patent. (Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 9-12, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019); *see* Ex. A, AIRM00290341-411, '551 patent at claim 5.)

148. In sum, comparing HB-MSCs to BM-MSCs as recited in claim 10 of the '956 patent and claim 21 of the '321 patent does not constitute a significant contribution to any claim of the '956 or '321 patents.

B. Astellas' Requested Rulings of Law on Inventorship

149. "A person who alleges that [he or she] is a co-inventor of the invention claimed in an issued patent who was not listed as an inventor on the patent may bring a cause of action to correct inventorship in a district court under 35 U.S.C. § 256." *Vapor Point LLC v. Moorhead*, 832 F.3d 1343, 1348 (Fed. Cir. 2016) (quoting *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1357 n.1 (Fed. Cir. 2004)), *cert. denied sub nom. Nanovapor Fuels Grp., Inc. v. Vapor Point, LLC*, 137

S. Ct. 1121 (2017); *see* 35 U.S.C. § 256 (2012) (permitting correction of inventorship "[w]henever . . . through error an inventor is not named in an issued patent").

150. "Inventorship is a mixed question of law and fact: The overall inventorship determination is a question of law, but it is premised on underlying questions of fact." *Eli Lilly*, 376 F.3d at 1362.

151. "Because the issuance of a patent creates a presumption that the named inventors are the true and only inventors, the burden of showing misjoinder or nonjoinder of inventors is a heavy one and must be proved by clear and convincing evidence." *Gen. Elec. Co. v. Wilkins*, 750 F.3d 1324, 1329 (Fed. Cir. 2014).

152. "In order to guard 'against courts being deceived by inventors who may be tempted to mischaracterize the events of the past through their testimony,' the law requires corroboration of a putative inventor's credible testimony, the sufficiency of which is measured under a 'rule of reason' standard." *Gen. Elec.*, 750 F.3d at 1330 (quoting *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1374 (Fed. Cir. 2009)); *GemStar-TV Guide Int'l, Inc. v. Int'l Trade Comm'n*, 383 F.3d 1352, 1382-83 (Fed. Cir. 2004).

153. "[I]n order for the rule of reason requirement to even apply there must be some evidence that a fact-finder can find reasonable; the putative inventor must first provide credible testimony that only then must be corroborated." *Gen. Elec.*, 750 F.3d at 1330 (citing *Univ. of Colorado Found., Inc. v. Am. Cyanamid Co.*, 342 F.3d 1298, 1308-09 (Fed. Cir. 2003)).

154. Reliance on "educational and employment backgrounds" for corroboration is "only weak circumstantial evidence with only a very attenuated relationship to [an alleged co-inventor's] potential contributions to the invention." *Gemstar-TV Guide Int'l,* 383 F.3d at 1382.

155. "To be a joint inventor, an individual must make a contribution to the conception of the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention." *Caterpillar Inc. v. Sturman Indus., Inc.*, 387 F.3d 1358 (Fed. Cir. 2004).

156. "Conception is the touchstone of inventorship, the completion of the mental part of invention. It is the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1227-28 (Fed. Cir. 1994).

157. Inventorship "requires more than merely exercising ordinary skill in the art—a person will not be a co-inventor if he or she does no more than explain to the real inventors concepts that are well known in the current state of the art." *Burroughs Wellcome Co.*, 40 F.3d at 1227-28 (alterations and citations omitted); *see also Gen. Elec.*, 750 F.3d at 1331-32 (where alleged co-inventor "conceded that the idea to use a UPS to perform LVRT was not novel in 2002," holding that even if the alleged co-inventor contributed "the idea to use a UPS, then he would have contributed nothing beyond what was already known in the art. That is not sufficient to name Wilkins as a co-inventor").

158. "A contribution of information in the prior art cannot give rise to joint inventorship because it is not a contribution to conception." *Eli Lilly*, 376 F.3d 1352, 1362 (Fed. Cir. 2004).

159. "One who merely suggests an idea of a result to be accomplished, rather than means of accomplishing it, is not a joint inventor." *Nartron Corp. V. Schukra U.S. A., Inc.*, 558 F.3d 1352, 1359 (Fed. Cir. 2009) (quoting *Garrett Corp. v. United States*, 422 F.2d 874, 881 (Ct. Cl. 1970)) (alterations and quotation marks omitted).

160. An alleged inventor's contribution is insignificant when the specification and claims of the patent-in-suit primarily focus on the named inventors' invention, and the specification mentions the alleged contribution only once in a twenty-column patent. *Nartron Corp.*, 558 F.3d at 1357-58.

1. Drs. Wang and Xu Are Not Co-inventors of the '551 Patent

161. Drs. Wang and Xu did not make a significant contribution to the conception of the claims of the '551 patent when their alleged contribution is measured against the claimed invention as a whole.

162. Consistent with this Court's findings on summary judgment, the specification of the '551 patent makes clear that the significance of the claimed invention in the '551 patent is the general method of making MSCs via an HB intermediate, which was contributed by Drs. Kimbrel and Lanza, and not any of the aspects that Defendants allege to have contributed.

163. Using a GSK3 inhibitor in the hESC culturing step does not amount to a significant contribution, as the specification of the '551 patent is devoted to Drs. Kimbrel and Lanza's HB-MSC method and mentions GSK3 inhibitors in only four places out of 68 columns of narrative text. Further, the '551 patent's specification explicitly states that use of such an inhibitor is an optional step and the entire '551 patent does not contain any data showing an effect of use of a GSK3 inhibitor on the end product HB-MSCs.

164. Defendants' alleged contributions to step (a) of claim 1 of the '551 patent are not significant as compared with Drs. Kimbrel and Lanza's HB-MSC method, also because they were already known and described in the scientific literature before Defendants' alleged conception. One cannot be a co-inventor by merely exercising ordinary skill in the art or explaining to the inventors the state of the art. *Hess v. Advanced Cardiovascular Sys., Inc.,*, 106 F.3d 976, 981 (Fed. Cir. 1997). Not only was feeder-free and serum-free culturing of hESCs well known in the art,

but Dr. Brivanlou and his colleagues had already discovered and reported use of the recited concentration of a GSK3 inhibitor, namely BIO, which is the only GSK3 inhibitor specifically identified in the '551 patent.

165. The concentration range recited in claim 1 of the '551 patent, which "is contained within a previously conceived broader range and is of no demonstrated significance," does not constitute an inventive contribution. *Mass. Eye & Ear Infirmary v. Novartis Ophthalmics, Inc.*, 199 F. App'x 960, 964 (Fed. Cir. 2006). In fact, Dr. Wang relied on Dr. Brivanlou's prior work to derive the idea of using the GSK3 inhibitor BIO at a concentration taught by Dr. Brivanlou. *See Nartron*, 558 F.3d at 1358 (rejecting inventorship claim where the alleged inventor researched and developed a particular embodiment that fell within a basic concept in the prior art). Despite acknowledging Dr. Brivanlou as the source of the idea to use GSK3 in his own notes, Dr. Wang later hid that connection, removing reference to Dr. Brivanlou in a presentation to other members of his laboratory. Even apart from the clear evidence that he had obtained the idea to use a GSK3 inhibitor from Dr. Brivanlou's prior publications, Dr. Wang's sparse, unwitnessed lab notebook pages do not evidence conception, as "unwitnessed laboratory notebooks on their own are insufficient to support his claim of co-inventorship." *Stern v. Trustees of Columbia Univ. in City of New York*, 434 F.3d 1375, 1378 (Fed. Cir. 2006). At best, Drs. Wang and Xu's inclusion of this technique explains well-known concepts or the state of the art at Defendants' purported conception date, and thus cannot be an inventive contribution to claim 1 of the '551 patent. *Caterpillar*, 387 F.3d at 1377.

166. The prosecution history of the '551 patent confirms the insignificance of the GSK3 inhibitor step, which was not even mentioned in the provisional patent applications to which the '551 patent claims priority and was described as only optional in the originally filed claims and

non-provisional application. Defendants narrowed their claim to require use of a GSK3 inhibitor during prosecution. The fact that a claim amendment adding the alleged contribution overcame rejections during prosecution does not support inventiveness where, as here, the teachings in the prior art "provide all that is necessary for one of skill in the art to identify the appropriate materials." *Caterpillar*, 387 F.3d at 1378. It is also telling that Dr. Brivanlou's 2006 and 2009 publications that taught the recited concentration of the GSK3 inhibitor were not submitted during prosecution for the examiner's consideration.

167. Thus, none of the four things that Defendants' initially alleged that they contributed to the '551 patent—(1) using a GSK3 inhibitor, specifically BIO, at a concentration range of 0.05 μM to 0.2 μM when culturing (2) "real, not MA09" hESCs under (3) feeder-free and (4) serum-free conditions—are significant when viewed in light of the invention as a whole.

168. After Astellas' opening expert reports on inventorship for the '551 patent were served, Defendants amended their allegations to add the allegations that they also contributed the IL-6 and mitotic inactivation features recited in certain claims of the '551 patent. (Ex. FB, Amend. Resp. to Interrog. No. 1 at pp. 9-12, Defs.' Amend. Obj. & Resp. to Astellas' First Set of Interrog. (Oct. 15, 2019).) Defendants then repeated their admission that "[t]he remaining dependent claims recite additional useful, but not independently inventive features. *Id.* These features, while not separately patentable, provide claims that are patentable, because as dependent claims, they automatically include the novel and inventive concepts of step (a)" of Claim 1. (*Id.* at p. 13.)

169. Regarding Defendants' belated allegation as to the IL-6 and mitotic inactivation features, Defendants should be bound by their admission in their earlier interrogatory responses that these features are "not independently inventive" and "not separately patentable." (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set

of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

170. Separately, as discussed *infra* ¶¶ 182 - 184 (incorporated here as if restated in full), Drs. Wang and Xu did not conceive of the IL-6 feature—Dr. Kimbrel did so before Defendants' first IL-6 experiments with HB-MSCs. Moreover, suggesting to investigate the amount of IL-6 expressed by the HB-MSCs made by Astellas' invention merely exercised ordinary skill in the art or explained to the inventors the state of the art. *Hess*, 106 F.3d at 981. IL-6 had been extensively characterized in MSCs from other sources in the prior art and widely understood in the field to play a role in multiple sclerosis and the EAE model.

171. Further, as discussed *infra* ¶¶ 185 - 186 (incorporated here as if restated in full), the mitotic inactivation feature is not an inventive contribution from Drs. Wang and Xu. Dr. Kimbrel had already shown that mitotically inactivated HB-MSCs maintained similar *in vitro* immunomodulatory effects to regular MSCs months before the first time Dr. Wang allegedly irradiated HB-MSCs. This supports that Drs. Wang and Xu were not the first to conceive mitotic inactivation of HB-MSCs. Moreover, one cannot be a co-inventor by merely exercising ordinary skill in the art or explaining to the inventors the state of the art. *Hess*, 106 F.3d at 981. By 2010, mitotic activation had been applied to many types of hESCs and cells derived from hESCs, including hESC-derived MSCs, to avoid the cells' well-known risk of tumor formation without compromising their immunomodulatory properties.

172. In sum, Drs. Wang and Xu did not make any significant contribution to any of the claims in the '551 patent. The Court has already held that Drs. Kimbrel and Lanza contributed significantly to '551 patent claims based on the core HB-MSC methodology, Defendants admit that most of the remaining elements of the claims "not independently inventive" and "not

separately patentable," and none of the features Drs. Wang and Xu allege to have contributed entitles them to inventorship on the '551 patent.

2. Drs. Wang Is Not a Co-inventor of the '956 Patent and Drs. Wang and Xu Are Not Co-inventors of the '321 Patent

173. Defendants fail to show by clear and convincing evidence that Dr. Wang should be a co-inventor of the '956 patent and that Drs. Wang and Xu should be co-inventors of the '321 patent.[7]

a. Dr. Wang is not a co-inventor of the '956 patent by conducting the routine EAE testing of Astellas' HB-MSCs

174. "[I]nvention turns on conception, not reduction to practice." *Bard Peripheral Vascular, Inc. v. W.L. Gore & Assocs., Inc.*, 670 F.3d 1171, 1201 (Fed. Cir. 2012) *opinion vacated in part on reconsideration*, 682 F.3d 1003 (Fed. Cir. 2012), *and vacated in part on reh'g en banc*, 476 F. App'x 747 (Fed. Cir. 2012). "[O]ne does not qualify as a joint inventor by merely assisting the actual inventor after conception of the claimed invention." *Eli Lilly*, 376 F.3d at 1359. Astellas' scientists had conceived the use of HB-MSCs for treating autoimmune disease and multiple sclerosis as claimed in the '956 patent before contacting and asking Dr. Wang to verify the immunotherapeutic properties of the HB-MSCs in the mouse EAE model. Moreover, the confirmatory EAE testing does not amount to an inventive contribution. At best, all Dr. Wang did was exercise ordinary skill in the art when running the well-known EAE test using Astellas' HB-MSCs.

175. An inventor "need not know that his invention will work for conception to be complete" and need not personally conduct all of the steps necessary to reduce the invention to

[7] As explained *supra* ¶ 125, Dr. Xu is precluded from asserting a claim to co-inventorship of the '956 patent.

practice—"what matters for conception is whether the inventors had a definite and permanent idea of the operative inventions." *Burroughs Wellcome*, 40 F.3d at 1230. Conducting animal studies verifying the inventor's conceived use of a novel compound to treat a disease is insufficient for co-inventorship. *Stern*, 434 F.3d 1375. A collaborator who performs testing that merely "amounted to screening and confirmation" of the effectiveness of the inventor's conceived novel compound is not an co-inventor. *Intercept Pharm., Inc. v. Fiorucci*, 277 F. Supp. 3d 678, 684 (D. Del. 2017). The same is true here, where simply confirming operability of the MSCs by performing the EAE tests is insufficient to support a claim of co-inventorship, especially when the expected properties of MSCs and the EAE model were already known in the art.

176. Defendants offer no evidence corroborating Drs. Wang and Xu's deposition testimony that they first suggested testing Astellas' HB-MSCs in the EAE model before Astellas scientists had set out to look for collaborators in standard animal models for autoimmune diseases. An alleged co-inventor must supply evidence to corroborate his own testimony of conception, even assuming his testimony was found credible. *Gemstar-TV Guide Int'l, Inc.*, 383 F.3d at 1382.

177. Educational and employment backgrounds are "only weak circumstantial evidence with only a very attenuated relationship to [an alleged inventor's] potential contributions to the invention." *Id.* at 1383.

178. Contemporaneous documents that fail to explicitly identify the alleged inventor's contribution or fail to show that the alleged contributions exceeded the prior art cannot surmount the clear and convincing evidentiary requirement. *Id.*

179. Alleged conception at the parties' meeting cannot support a claim of co-inventorship absent corroboration with written documentation of the communication. *Eli Lilly*, 376 F.3d at 1363; *Ferring B.V. v. Allergan, Inc.*, No. 12-CV-2650 (PKC), 2019 WL 6183501, at

*14-15 (S.D.N.Y. Sept. 27, 2019). A follow-up email cannot cure the insufficient corroboration if it does not clearly record the alleged communication from the prior meeting. *Id.* There is no written record of what Dr. Lu discussed with Dr. Xu at the June 2010 ISSCR conference or at his July 13, 2020 meeting with Drs. Wang and Xu at Astellas. It is even unclear whether Dr. Wang was present at the June 2010 meeting. Dr. Wang's Summer 2010 emails to Astellas' scientists do not show that Dr. Wang conceived the use of Astellas' HB-MSCs for treating autoimmune diseases before Astellas scientists already did so. Moreover, on November 18, 2011, Dr. Kimbrel told Defendants that "ACT is particularly interested in developing our MA09-MSCs as a therapeutic product" and, "[i]n fact, a patent application for our MSCs is already being drafted." (Ex. 13, IMSTEM-0004720-721 at IMSTEM-0004721; Xu Dep. at 110:1-9). Yet, Dr. Wang did not assert an inventorship claim at this time. Instead, he waited for years—until after Astellas brought suit to correct inventorship on the '551 patent, to finally raise an inventorship claim.

180. Even assuming that Dr. Wang first told Drs. Kimbrel and Lanza about the potential to use their MSCs to treat multiple sclerosis or EAE, that idea is nothing novel or inventive. Where the alleged co-inventor contributes "only well-known principles," those contributions "do not constitute the conception necessary to establish co-inventorship." *Applied Elastomerics, Inc. v. Z-Man Fishing Prods., Inc.*, 521 F. Supp. 2d 1031, 1042 (N.D. Cal. 2007); *see also Caterpillar Inc.*, 387 F.3d at 1378 (noting "various publicly available texts and patents described" the contribution of the purported coinventor); *Ruling Meng v. Ching-Wu Paul Chu*, 643 F. App'x 990, 996 (Fed. Cir. 2016) (rejecting inventorship where plaintiff synthesized claimed superconducting compounds using methods which were ordinary skill in her profession); *Hess*, 106 F.3d at 981 (plaintiff was not an inventor by explaining principles that "were well known and found in textbooks"). Dr. Wang's alleged contribution does not exceed the level of ordinary skill in the art

and is legally insufficient to support Defendants' claim for co-inventorship of the '956 patent. The inclusion of the EAE data in the '956 patent specification does not justify Dr. Wang's inventorship as it does not demonstrate a contribution to conception of the invention. Moreover, inventorship "is determined by contribution to the claims, not to the specification." *Intermec Techs. Corp. v. Palm Inc.*, 738 F. Supp. 2d 522, 563 (D. Del. 2010)), *aff'd*, 466 F. App'x 881 (Fed Cir. 2012). To the extent Defendants assert that Dr. Wang performed "excessive" experimentation to supply the EAE data in the '956 patent, the quantity of work does not demonstrate that he exceeded ordinary skill in the art. *Meng*, 643 F. App'x at 996.

181. While Dr. Wang is a co-first-author with Dr. Kimbrel on the parties' collaborative paper, authorship "by itself does not raise a presumption of inventorship." *In re Katz*, 687 F.2d 450, 455 (C.C.P.A. 1982). An alleged inventor's being listed as a first author at most shows that he had a substantial involvement in the collaboration, "but can neither prove nor disprove that he contributed to the specific idea of" the claimed feature. *Meng*, 643 F. App'x at 996. Dr. Wang's authorship does not mean that he made any inventive contribution to Astellas' conceived use of its cells expressed in the Astellas patents.

b. Dr. Wang is not a co-inventor of the '956 patent (or the '551 patent) by suggesting to test IL-6 expression from Astellas' HB-MSCs

182. As a preliminary matter, Drs. Wang and Xu essentially admitted that they contributed nothing to the novel HB-MSCs at the core of the '956 and '321 patents and thus do not qualify to be named as co-inventors. *See Irwin Indus. Tool Co. v. Bibow Indus., Inc.*, No. CIV.A. 11-30023-DPW, 2012 WL 5420033, at *4 (D. Mass. Nov. 6, 2012)), *aff'd*, 530 F. App'x 965 (Fed. Cir. 2013) (finding the purported co-inventor's contribution "did not involve the core innovation" of the patent in suit); *Nartron Corp.*, 558 F.3d at 1358 (even contributing the sole

limitation of one dependent claim was not significant in the context of the entire invention, where the alleged co-inventor did not contribute anything to the underlying independent claim).

183. Dr. Wang admitted that the only significant invention in any of the patents was the method of making HB-MSCs when he acknowledged in interrogatory responses that nothing beyond claim 1 of the '551 patent constituted more than "useful but not independently inventive" additions.[8] This statement specifically disavowed the notion that identification of IL-6 expression levels constituted a separate inventive contribution.

184. The documentary evidence shows that Dr. Wang did not conceive of the idea to test the IL-6 expression level as claimed in the '956 patent.[9] It was Dr. Kimbrel who first designed a targeted antibody array and discovered low IL-6 expression in the HB-MSCs months before Dr. Wang's microarray testing. The fact that the named inventor's experiment record of the claimed feature is dated earlier shows that the alleged inventor was not first to conceive that feature. *Meng*, 643 F. App'x at 995. Here, Dr. Kimbrel's earlier discovery of low IL-6 expression in the HB-MSCs counsels against Dr. Wang's alleged conception. Moreover, one cannot be a co-inventor by merely exercising ordinary skill in the art or explaining to the inventors the state of the art. *Hess*, 106 F.3d at 981. IL-6 had been extensively characterized in MSCs from other sources in the prior art and widely understood in the field to play a role in multiple sclerosis and the EAE model. Setting aside that Dr. Kimbrel decided to test for IL-6 expression first, Dr. Wang's characterization of the IL-6 expression level of HB-MSCs merely followed the prior art practice, and thus cannot

[8] Dr. Wang's later effort to disavow his sworn interrogatory answer should be discounted as litigation-driven and given no weight.

[9] The same conclusions of law apply to deny Drs. Wang and Xu's co-inventorship of the '551 patent based on the alleged contributions of IL-6.

support Dr. Wang's claim of co-inventorship of the '551 patent. *See, e.g.*, *Caterpillar*, 387 F.3d at 1377.

c. Dr. Wang is not a co-inventor of the '956 patent and Drs. Wang and Xu are not co-inventors of the '321 patent (or the '551 patent) by suggesting to mitotically inactivate Astellas' HB-MSCs

185. As a preliminary matter, Drs. Wang and Xu essentially admitted that they contributed nothing to the novel HB-MSCs at the core of the '956 and '321 patents and thus do not qualify to be named as co-inventors. *See Irwin Indus. Tool Co.*, 2012 WL 5420033, at *4 (finding the purported co-inventor's contribution "did not involve the core innovation" of the patent in suit); *Nartron Corp.*, 558 F.3d at 1358 (even contributing the sole limitation of one dependent claim was not significant in the context of the entire invention, where the alleged co-inventor did not contribute anything to the underlying independent claim). Defendants admitted in March 2019, and should be bound by this admission, that the mitotic inactivation feature is "not independently inventive" and "not separately patentable." (Ex. V, Resp. to Interrog. No. 1 at p. 8, Defs.' Xiaofang Wang and ImStem's Resp. to Astellas' First Set of Interrog. (Mar. 6, 2019); Ex. GQ, Resp. to Interrog. No. 1 at p. 8, Def. Ren-He Xu's Resp. to Astellas' First Set of Interrog. (Mar. 7, 2019).)

186. Drs. Wang and Xu did not make any significant contribution to the concept of mitotic inactivation as claimed in the '956 and '321 patents.[10] Dr. Kimbrel had already shown that mitotically inactivated HB-MSCs maintained similar *in vitro* immunomodulatory effects to regular MSCs months before the first time Dr. Wang allegedly irradiated HB-MSCs. This supports that Drs. Wang and Xu were not the first to conceive mitotic inactivation of HB-MSCs. Further, one

[10] The same conclusions of law apply to deny Drs. Wang and Xu's co-inventorship of the '551 patent based on the alleged contributions of mitotic inactivation.

cannot be a co-inventor by merely exercising ordinary skill in the art or explaining to the inventors the state of the art. *Hess*, 106 F.3d at 981. By 2010, mitotic activation had been applied to many types of hESCs and cells derived from hESCs, including hESC-derived MSCs, to avoid the cells' well-known risk of tumor formation without compromising their immunomodulatory properties. Suggesting use of this well-known technique in the claims does not qualify Drs. Wang as a co-inventor on the '956 patent or Drs. Wang and Xu as co-inventors of the '321 patent (or the '551 patent). *See, e.g., Caterpillar*, 387 F.3d at 1377.

d. Dr. Wang is not a co-inventor of the '956 patent and Drs. Wang and Xu are not co-inventors on the '321 patent (or the '551 patent) by suggesting to compare Astellas' HB-MSCs with BM-MSCs

187. As a preliminary matter, Drs. Wang and Xu essentially admitted that they contributed nothing to the novel HB-MSCs at the core of the '956 and '321 patents and thus do not qualify to be named as co-inventors. *See Irwin Indus. Tool Co.*, 2012 WL 5420033, at *4 (finding the purported co-inventor's contribution "did not involve the core innovation" of the patent in suit); *Nartron Corp.*, 558 F.3d at 1358 (even contributing the sole limitation of one dependent claim was not significant in the context of the entire invention, where the alleged co-inventor did not contribute anything to the underlying independent claim).

188. Drs. Wang and Xu did not make any significant contribution to the concept of comparing Astellas' new type of MSCs, HB-MSCs, with BM-MSCs. Comparing a new type of MSCs with BM-MSCs had been widely practiced in the prior art before the parties' collaboration. Defendants' own grant application and email admitted that the comparison was nothing beyond the prior art knowledge. Drs. Wang did not make a significant contribution to any claim of the '956 patent and Drs. Wang and Xu did not make a significant contribution to any claim of the '321

patent (or the '551 patent) by suggesting or conducting a comparison widely known in the art and thus the do not qualify as co-inventors of these patents. *See, e.g., Caterpillar*, 387 F.3d at 1377.

II. STATE LAW CLAIMS

A. Astellas' State Law Claims

189. Astellas' state law claims generally arise from the same series of events and common facts. Below, Astellas sets forth its proposed findings of fact that underlie all its state law claims in the section for Unfair Trade Practices, and then incorporates these facts by reference for Astellas' unjust enrichment and conversion claims.

1. Unfair Trade Practices (Massachusetts General Laws Chapter 93A)

a. Astellas' Proposed Findings of Fact on Astellas' Unfair Trade Practices Claim

190. As discussed above in Section I.A. (¶¶ 5 - 148, incorporated here as if restated in full), Astellas had already invented the novel HB-MSC method before ever meeting with Defendants. Because Astellas (then ACT and SCRMI) was a small company back in 2010 with limited employees and resources and without access to animal testing facilities, Astellas embarked to look for collaborators to confirm its proposed therapeutic uses of the HB-MSCs, including the use for treating autoimmune diseases such as multiple sclerosis. In July 2010, Astellas engaged Dr. Lu's friend, Dr. Xu, then a professor at the University of Connecticut ("UConn"), and Dr. Xu's then-postdoc Dr. Wang to verify this use in a standard animal model for multiple sclerosis called EAE. (Ex. 50, AIRM00013841-60 at AIRM00013841-42).

191. The parties entered into an academic collaboration to support Astellas' drug development, with the understanding that the final end result would be a joint paper. (*See* Kimbrel Dep. at 153:21-24, 224:11-19; Ex. 27, IMSTEM-0005466-468 (discussing sharing data for joint paper).) Dr. Xu admitted that for such an academic collaboration, Defendants had the basic

understanding that any information that Astellas shared during the collaboration would be kept confidential. (Xu. Dep. at 68:17-69:2 ("Q. You understood that because it was an academic style collaboration, that you shouldn't disclose or provide to others the materials they provided to you, the cells and the protocols, right? A. In general, we should have this kind of for basic understanding. Yeah. But specifically what the protocol, what the cells, I think, as I told you, I totally rely on Xiaofang Wang to."))

192. In addition to this basic understanding, Astellas reiterated several times over the course of the collaboration that all shared information was proprietary, confidential, and for the limited purpose of the collaboration. On March 28, 2011, Dr. Kimbrel shared some of her MSC data ("trilineage differentiation" data) with Dr. Wang on the following express premises: "As we are a company and have not yet filed our patent for the MSC stuff, please DO NOT distribute the slides to anyone else. The data should only be used for your internal departmental presentations or Xu lab meetings. Please please do not use the data for any other purposes. This is very important for our viability as a company!" (Ex. 39, IMSTEM-0002553-556 at IMSTEM-0002553.) Dr. Wang agreed that they "will only use it for departmental presentation" and Dr. Kimbrel thanked him "for understanding about the confidentiality." (*Id.*) On November 18, 2011, Kimbrel told Defendants that "ACT is particularly interested in developing our MA09-MSCs as a therapeutic product" and, "[i]n fact, a patent application for our MSCs is already being drafted." (Ex. 13, IMSTEM-0004720-721 at IMSTEM-0004721; Xu Dep. at 110:1-9). Astellas filed its patent application shortly thereafter on November 30, 2011, as Provisional Patent Application No. 61/565,358. (Ex. 35.) Defendants said nothing at the time about seeking a patent of their own or being included in the Astellas patent.

193. On December 9, 2011, Dr. Kimbrel put their understanding of the confidentiality and use of the shared information in writing: "Due to legal implications and intellectual property rights concerning the very use of our hemangioblast-derived MSCs, we need to to [sic] clearly define and agree upon the intended use of our cells, endpoints of the study, authorship, and itemized budget. . . . Detailed, proprietary protocols, cells, and preliminary data offered by ACT must be kept in the strictest of confidence. Collaborators are NOT to share any cells or protocols with third parties without the explicit written consent of ACT. . . . Please respond via email and let us know if you agree to the above terms." (Ex. 25, IMSTEM-0004606-607.) Dr. Xu replied on the same day stating: "Thanks for the update I don't think I have any problem with these." (*Id.* at IMSTEM-0004606; *see also* Xu Dep. at 116:15-20 (describing his understanding of this agreement).)

194. On April 2, 2012, Dr. Kimbrel emailed Dr. Wang about the need to split the work into two papers, explaining that Drs. Wang and Xu could be co-authors on the methods paper and that Astellas would share *in vitro* data for use in the EAE paper. (Ex. 27, IMSTEM-0005466-468.) Dr. Kimbrel stated that "[a]s long as you acknowledge and agree to this upfront, we can share our findings with you . . . I suppose our company's very existence depends upon maintaining control of proprietary methodology that we generate here." (*Id.*) Drs. Xu and Wang agreed. (*Id.* at IMSTEM-0005466; Ex. GT, IMSTEM-0005455-457 at IMSTEM-0005456.)

195. Defendants repeatedly promised Astellas confidentiality and that they would not use the shared materials outside the collaboration without Astellas' explicit permission. Drs. Wang and Xu were university researchers at the time and were viewed as academic colleagues not commercial competitors by the Astellas scientists.

196. Nothing in the relationship between the Parties suggested that Drs. Wang or Xu would gain the rights to file their own patent application, much less found a commercial venture, based on information provided by Astellas. Relying on Defendants' repeated assurance of confidentiality, Astellas shared its method, cells, data, and know-how with Defendants over the years of collaboration, under the assumption that the information would not be misused for the purposes outside of the collaboration.

197. For example, after an initial meeting with Dr. Lu on July 12, 2010, Dr. Wang asked Dr. Lu for a contact to get MSC protocols and cells. Dr. Lu introduced Dr. Kimbrel, who had already generated HB-MSCs that were ready for testing. (*Id.*) On July 29, 2010, Dr. Kimbrel emailed Dr. Wang regarding a potential collaboration on "the use of our hemangioblast-derived MSCs in the treatment of autoimmune diseases." (Ex. 11, IMSTEM-0001523-530 at IMSTEM-0001526). When meeting with Defendants to discuss collaboration details at Astellas on August 11, 2010, Dr. Kimbrel gave Defendants Astellas' MA09 HB-MSCs to begin their confirmatory testing. (*See id.* at IMSTEM-0001524; Wang Dep. at 237:5-12.) On the same day, Dr. Kimbrel emailed Dr. Wang her confidential protocol for making HB-MSCs, which included brand new steps and non-public changes in an attached protocol labeled "Confidential, do not distribute!" (Ex. 11, IMSTEM-0001523-530 at IMSTEM-0001523, 528.) When Drs. Wang and Xu received this information, they understood that it was confidential and should not be shared or used outside the collaboration. (Wang Dep. at 97:11-98:1 ("Q. So you understood when you received this that this was a confidential protocol that you were being provided, right? A. Yes."); *see also, e.g.*, Ex. 39, IMSTEM-0002553-556 (on March 28, 2011, Dr. Kimbrel sharing confidential MSC data with Dr. Wang for internal departmental presentations); Ex. GX, IMSTEM-0009014-015 (on April 23, 2012, Drs. Kimbrel and Kouris driving to UConn deliver MA09-MSCs to Dr. Wang); Ex. GU,

IMSTEM-0005999-6001 (on August 23, 2012, Astellas approving $10,000 budget upon Dr. Wang's request to order reagents); Ex. GV, IMSTEM-0006192 (on January 28, 2013, Dr. Kimbrel ordering more EAE induction kits for Dr. Wang).)

198. While agreeing to treat Astellas' technology as confidential and to use it only for the collaboration and outwardly appearing to work collaboratively with Astellas, Defendants broke their promises of confidentiality and took far more than they were entitled to by claiming Astellas' technology as their own and using it in patent filings, grant applications, business plans and presentations, and to jump start their T-MSC work.

199. Defendants disclosed and claimed Astellas' technology in the '551 patent and applications to which the '551 patent claims priority. The Court has already found on summary judgment that "Defendants admit that Plaintiffs shared their protocol prior to it becoming public and that the protocol appears in Defendants' '551 patent." (Dkt. 163 at 8.) As discussed above in Section I.A.1 (**¶¶** 5 - 72**Error! Reference source not found.**), the '551 patent focuses on the significance of Astellas' HB-MSC method and relies on data using HB-MSCs generated via Astellas' method, including data using the MA09 HB-MSCs that Defendants received directly from Astellas during the collaboration.

200. Defendants never informed Astellas that they had filed patents on HB-MSC technology. (Wang Dep. 223:10-16, 224:10-18; Xu Dep. 187:7-14.)

201. During the prosecution of the '551 patent in January 2017, Drs. Wang and Xu submitted a declaration sworn under the penalty of perjury that they were the "original and joint inventors" of Astellas' HB-MSC method and that they "had possession of the Invention in the United States of America before November 30, 2011. . . ." (Ex. 29, AIRM00295774-810 at AIRM00295784.)

202. Further, Defendants contemporary emails regarding applications leading to the '551 patent demonstrated their intent to use their filings to block Astellas' use of its own HB-MSC technology. On July 3, 2012, Dr. Wang circulated a draft provisional patent application to Dr. Xu and their business contact and later investor for ImStem, Mr. Michael Men. Dr. Wang acknowledged that the patent was directed to Astellas' inventions and not his own, stating that "this patent is to prevent [Astellas] from using their technology to go to clinic and develop product." (Ex. Z, IMSTEM-0031515-532 at IMSTEM-0031515.)

203. On July 9, 2012, Dr. Wang circulated the draft patent application again, stating he added "more claims for our attack patent." (Ex. AA, IMSTEM-0027835-843 at IMSTEM-0027835.)

204. On July 13, 2012, one day after filing their provisional application with the USPTO, Dr. Wang sent Dr. Xu an HB-MSC invention disclosure form to be submitted to UConn, which detailed the method to make HB-MSCs again using the confidential protocol provided by Dr. Kimbrel. (Ex. 14, IMSTEM-0009108-125 at IMSTEM-0009114.) Where the form instructed to "describe any materials obtained from third parties (such as research collaborators or companies with or without a Material Transfer Agreement) that were used in the development of the invention," Defendants wrote "None." (*Id.* at IMSTEM-0009118.) In his cover email to only Dr. Xu (not any UConn official), Dr. Wang described the invention disclosed in the attached form as one where: "We will have paper submitted soon for this one in collaborate [sic] with [Astellas]" and "we may file this [patent] and ask for royalty from [Astellas] if they have successfully marketing [sic] their product." (*Id.* at IMSTEM-0009108.)

205. On July 14, 2012, Dr. Xu submitted this invention disclosure form, which answered "None" in response to the instruction to describe any third party materials such as those obtained

from research collaborators that were used in developing the invention, to UConn. (Ex. Y, IMSTEM-0005543-559 at IMSTEM-0005543.) At his deposition, Dr. Xu testified that he and Dr. Wang told UConn that they "have a collaboration" with Astellas regarding HB-MSCs. (Xu Dep. Tr. 212:8-16, 212:18-20.) But no record exists of such a communication.

206. Defendants intentionally hid Astellas' original development of the HB-MSC method from UConn when they first filed the '551 patent and from the USPTO in 2017 to secure the issuance of the patent.

207. Defendants misused Astellas' technology to solicit business and investments to form a competing business. On September 7, 2011, Dr. Wang emailed Dr. Xu a business strategy presentation based on Astellas' HB-MSC technology with a "strategy in China" by establishing a U.S. research company to provide technical support to a Chinese company backed by Chinese government support. (Ex. AK, IMSTEM-0008577-578 (translation at AIRM00296707-740).)

208. On March 12, 2012, Drs. Xu and Wang sent Mr. Men a business proposal for ImStem, which described ImStem's technology as MSCs differentiated "through embryoid bodies and then hemangioblasts" and identified Astellas (then ACT) a one of two major competitors, without mentioning anything about GSK3 inhibitors or T-MSCs. (Ex. 19, IMSTEM-0040434-453.)

209. On April 2, 2012, the very day that Dr. Xu agreed to Dr. Kimbrel's email about sharing Astellas' data only for the joint paper, Drs. Xu and Wang emailed among themselves about a patent search report monitoring patent filings by their "two major competitor[s]," one of which was ACT, Astellas' predecessor. (*Compare* Dr. Xu's reply to Dr. Kimbrel at 4:19:51 PM April 2, 2012 (Ex. 27, IMSTEM-0005466-468 at IMSTEM-0005466), *with* Dr. Xu's email to Dr. Wang at 12 PM on the same day (Ex. 26, IMSTEM-0040416-421 at IMSTEM-0040416).)

210. Subsequently, Drs. Wang and Xu, along with investor Mr. Men, formed ImStem around June 2012. (Ex. 18, IMSTEM-0040593-601.)

211. Defendants also formed Zhuhai Hengqin ImStem Biotechnology Co., Ltd. ("Zhuhai ImStem"), a Chinese corporation that pays Defendant ImStem for services. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019); Ex. MG, Resp. to Interrog. No. 28, Def. Xu's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019).)

212. Defendant Wang and Michael Men work at both Defendant ImStem and Zhuhai ImStem. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019); Ex. MG, Resp. to Interrog. No. 28, Def. Xu's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019).)

213. Michael Men is the Acting Chief Executive Officer of Defendant ImStem and the Chief Executive Officer of Zhuhai ImStem. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019); Ex. MG, Resp. to Interrog. No. 28, Def. Xu's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019).)

214. Defendant Wang also holds a consulting role with Zhuhai ImStem. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019).)

215. Defendant Xu currently holds shares of Defendant ImStem and Zhuhai ImStem.

216. On October 16, 2017, Defendant ImStem transferred the rights to a Chinese patent claiming priority to the '787 and '961 provisionals and to PCT Application No. PCT/US2013/048291, to which the '551 patent claims priority, to Zhuhai ImStem. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' 2nd Set of Interrog. (July 16, 2019).)

Defendants did not compensate Astellas, Dr. Kimbrel, or Dr. Lanza in connection with this transfer of rights.

217. Defendants also misused Astellas' technology to apply for several grants for their own. For example, Drs. Wang and Xu submitted a grant application in the name of ImStem to a Connecticut granting agency based on Astellas' HB-MSC method, without mentioning Astellas. This grant application did not discuss or include anything about GSK inhibitors or T-MSCs. (Ex. AV, IMSTEM-0018362-462 at IMSTEM-0018373, -376.) Defendants were awarded about $1.13 million for this grant and continued to enjoy funding from this grant up to at least October 2016. (Ex. AI, IMSTEM-0021598-625 at IMSTEM-0021607.)

218. Defendants also misused Astellas' technology to jump start their own work on MSCs derived from trophoblast cells, so called "T-MSCs." Defendants gained access to Astellas' novel HB-MSCs and methods, and used the information as a "shortcut" to perform their own further work, which eventually became the basis of their patent applications, grants and their new business, ImStem. (*See* Xu. Dep. at 80:10-13 ("So only because ACT had the cells ready, available, somebody is working on it. So we then think, you know, maybe it's shortcut so we can use these cells right away"); *id.* at 75:14-17 ("their company is making –generating MSCs from ES cells, and so I think that will give us a shortcut to do the test."); *id.* at 82:3-8 ("ACT just give us the shortcut to have the cells").

219. Dr. Xu admitted that they used HB-MSCs to establish concepts for other cell types, including their TMSCs. (*See* Xu Dep. at 322:8-324:7.) Defendants' 2016 progress report to the state of Connecticut for the grant discussed *supra* ¶ 217 demonstrated their progress partly by pointing to the Parties' joint paper in Stem Cell Reports in 2014, which used Astellas' HB-MSC method. Defendants also stated in their 2016 progress report that they developed their T-MSC

product IMS001 targeting multiple sclerosis based on the work disclosed in the Stem Cell Reports article. (Ex. AI, IMSTEM-0021598-625 at IMSTEM-0021601.)

220. Defendants' later materials sent to potential investors and ImStem's current website continue to list the '551 patent to tout ImStem's MSC technology. (Ex. AJ, IMSTEM-0023976-009 at IMSTEM-0023985; Ex. GH, AIRM00298877.)

221. When the collaboration ended shortly after the parties published their joint paper in June 2014 (Ex. 9, AIRM00289980-995), Astellas had spent a considerable amount of employee time and costs to further Defendants led Astellas to believe was a mutually beneficial collaboration. Astellas' collaborative efforts included over 8,000 total man-hours, at least $10,000 worth of reagents, particularly with Dr. Kimbrel spending almost half of her time over several years working with Defendants and delivering HB-MSC cells to Defendants at UConn over ten times herself or with the help of her Astellas colleagues. (*See* Ex. DE, Summary of Time Spent; Ex. GU, IMSTEM-0005999-6001.)

222. Unbeknownst to Astellas, Defendants disavowed their promises of confidentiality and limited use. Not only did Defendants impair Astellas' intellectual property rights, but they explicitly plotted to delay Astellas' work for the benefit of ImStem. (*See* Ex. 20, IMSTEM-0031133-134 (upon Astellas' request for EAE experiments in August 2013, Dr. Wang stating to Mr. Men that "I will keep this under UConn for now and delay them a couple of months[,] so there is no interaction between ImStem and act so far" while telling Dr. Kimbrel that they could not start the experiment until October for various reasons).)

(1) Monetary damage to Astellas due to Defendants' Unfair Trade Practices

223. Before they began collaborating with Astellas in July 2010, Defendants had no experience making MSCs from ESCs. (Wang Dep. Tr. at 282:23-285:4.)

224. Defendants' access to Astellas' HB-MSC technology was limited to the purpose of the collaboration. (Ex. 39, IMSTEM-0002553-556 at -553.)

225. Defendants were informed that they must keep Astellas' HB-MSC technology confidential. (Ex. 25, IMSTEM-0004606-607 at -606-607.)

226. Defendants began efforts to commercially exploit Astellas' HB-MSC technology at least by September 2011. (Ex. AK, IMSTEM-0008577-578 (translation at AIRM00296707-740).)

227. Defendants began forming their own company based on Astellas' HB-MSC method and preclinical data as early as March 2012. (Ex. GL, IMSTEM-0040473-491.)

228. Defendants' company, ImStem, was incorporated on June 1, 2012. (Ex. 18, IMSTEM-0040593-601.)

229. Defendants' company relied on the use of Astellas' HB-MSCs to treat autoimmune diseases as a basis for its formation. (Ex. GL, IMSTEM-0040473-491 at -479.)

230. Defendants identified that Astellas' predecessor was expected to be a direct competitor for their newly formed company in ESC-derived MSCs. (Ex. 19, IMSTEM-0040434-53 at -444-45.)

231. Defendants relied on its patent filed in July 2012 on Astellas' HB-MSC technology to solicit investments. (Ex. AJ, IMSTEM-0023976-009 at -976.)

232. Astellas' patent application was published on June 6, 2013. (Ex. 3 AIRM00296616.)

233. The publication of Astellas' patent application was the first time that some of the confidential information about Astellas' HB-MSCs was publicly disclosed. (*see* Dkt. 129-22 at p. 20, Bell Rpt. at ¶ 44; *see* Ex. 3, AIRM00296616-646; Kimbrel Dep. at 262:2-263:13.)

234. Prior to the publication of Astellas' patent application, Astellas expected to be in complete control of access to its HB-MSC technology. (Ex. 39, IMSTEM-0002553-556.)

235. But-for Defendants misuse of their access to Astellas' HB-MSC technology, Astellas would have been the only commercial entity in the market for ESC-derived MSCs based on their technology. (*see* Dkt. 129-22 at p. 19, Bell Rpt. at ¶ 43; Bell Dep. Tr. at 147:16-148:9.)

236. Defendants used their access to Astellas' HB-MSC technology to form a direct competitor to Astellas in ESC-derived MSCs. (*See, e.g.*, Ex. 19, IMSTEM-0040434-53 at -440-45.)

237. Defendants used their access to Astellas' HB-MSC technology as a "short cut" to establish a direct competitor to Astellas. (Xu. Dep. Tr. at 75:14-17, 80:10-13.)

238. The commercial potential for ImStem's ESC-derived MSCs do not appear to be associated with any scientific advantages as compared to Astellas' HB-MSCs. (Wang Dep. Tr. at 254:19-20, 255:6-9.)

239. The value of ImStem in June 2013 reflects the amount by which Astellas was damaged from Defendants' unfair trade practices.

240. On June 22, 2013, ImStem received three equity investments totaling $593,000.

241. The $593,000 equity investments were received in exchange for 593,000 shares of ImStem. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

242. These 593,000 shares constituted 37% of the 1,603,000 ImStem shares outstanding. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

243. Investments totaling $593,000 for a 37% stake in ImStem implies a total value of $1,603,000.

244. Astellas was damaged by at least $1.6 million as a result of Defendants' unfair trade practices.

b. Astellas' Requested Rulings of Law on Astellas' Unfair Trade Practices Claim

245. "Unfair methods of competition and unfair or deceptive acts or practices in the conduct of any trade or commerce are hereby declared unlawful." Mass. Gen. Laws. ch. 93A, §§ 2, 11. In determining whether a practice violates Chapter 93A, courts look to "(1) whether the practice is within at least the penumbra of some common-law, statutory, or other established concept of unfairness; (2) whether it is immoral, unethical, oppressive, or unscrupulous; and (3) whether it causes substantial injury to consumers (or competitors or other businessmen)." *Mass. Eye & Ear Infirmary v. QLT Phototherapeutics, Inc.*, 552 F.3d 47, 69 (1st Cir. 2009), *decision clarified on denial of reh'g*, 559 F.3d 1 (1st Cir. 2009) ("*MEEI II*").

246. For a particular act or action to be unfair or deceptive, it does not need to violate common or statutory law; rather, Massachusetts courts evaluate unfair and deceptive trade practice claims based on the circumstances of each case. *Id.* (citing *Kattar v. Demoulas*, 739 N.E.2d 246, 257 (2000)).

247. In weighing an act's fairness, the focus is "on the nature of the challenged conduct and on the purpose and effect of that conduct as the crucial factors." *Damon v. Sun Co.*, 87 F.3d 1467, 1483-84 (1st Cir.1996) (quoting *Mass. Employers Ins. Exch. v. Propac–Mass, Inc.*, 648 N.E.2d 435, 438 (1995)).

248. Defendants committed unfair or deceptive acts by misappropriating Astellas' technology under the guise of an academic collaboration and misusing Astellas' technology for commercial gain.

249. Misuse of confidential information can support Chapter 93A liability. *MEEI II*, 552 F.3d at 71.

250. Defendants admitted that they had a general understanding of confidentiality underlying an academic collaboration like the one at issue. When Astellas reminded Defendants several times that the cells, methods, and data Astellas shared were confidential and could only be used for the limited purposes of the collaboration, Defendants repeatedly promised to keep confidential and not to misuse the shared materials. Yet Defendants went behind Astellas' backs to include Astellas' confidential information in patent filings, grant applications, business plans, and investor presentations, and to rely on Astellas' technology to jump start their T-MSC work.

251. The Court has already found on summary judgment that "Defendants admit that Plaintiffs shared their protocol prior to it becoming public and that the protocol appears in Defendants' '551 patent." (Dkt. 163 at 8.)

252. Defendants' internal emails evidenced the unfair and deceptive nature of their acts. Defendants admitted that they filed the '551 patent as an "attack patent" to "prevent [Astellas] from using their technology to go to clinic and develop product" and to "ask for royalty from [Astellas] if they have successfully marketing [sic] their product." Defendants hid the fact that it was Astellas who developed the HB-MSC technology from not only their business partners and investors, but also their previous employer University of Connecticut, the state funding agency of Connecticut responsible for awarding Defendants' grant, and, more recently in 2017, the USPTO. Even today, Defendants still list the '551 patent on ImStem's website to promote their T-MSC business.

253. Further, "stringing along" a counterparty—even a sophisticated one (which Astellas was not at the time of the collaboration)—to induce detrimental reliance can constitute a

Chapter 93A violation. *MEEI II*, 552 F.3d at 70 (citing *Greenstein v. Flatley*, 474 N.E.2d 1130, 1133 (1985)).

254. Defendants' repeated false promises to Astellas induced Astellas to detrimentally rely on such promises to continue to supply materials and technical know-how to Defendants over the years to further what appeared, at the time, to be an equal-footing collaboration. Unbeknownst to Astellas, Defendants had always treated Astellas as a major competitor—even doing so on the same day that they agreed to Astellas' emailed terms for confidentiality. Further, they secretly schemed to delay work for Astellas for the benefit of ImStem.

255. Similar to the conduct found egregious in *MEEI*, Defendants secretly enjoyed a "shortcut" from misusing Astellas' technology; without the benefits that they extracted from Astellas, Defendants "would have had to expend considerably greater sweat and treasure" to develop their T-MSC product. *Id.* at 70-71. Even more egregiously, Defendants continued to assure Astellas that they would safeguard Astellas' confidential information and materials even as they were disclosing them and using them to file their own patents, seek their own funding, start their own company, and plot against Astellas.

256. Defendants' practice caused substantial injury to Astellas. Astellas was injured by having their intellectual property rights to MSCs impaired and having its time and money misused in furthering a collaboration that was not, in fact, mutually beneficial. Defendants injured Astellas in the commercial realm by taking Astellas' intellectual property for free, denying Astellas the compensation it would otherwise have charged a competitor to use the technology, growing their own business from an unwittingly granted "shortcut," and blocking Astellas from enjoying the full scope of its technology. Astellas should also be granted equitable relief in the form of return all

intellectual property rights that contain its MSC technology, including all patents and applications Defendants have filed, worldwide, that contain Astellas' MSC technology.

2. Unjust Enrichment

a. Astellas' Proposed Findings of Fact on Astellas' Unjust Enrichment Claim

257. Astellas incorporates its proposed findings of fact from Section II.A.1.a (¶¶ 190-244) here as if restated in full.

(1) Monetary value by which Defendants were unjustly enriched

258. Before they began collaborating with Astellas in July 2010, Defendants had no experience making MSCs from ESCs. (Wang Dep. Tr. at 282:23-285:4.)

259. Defendants' access to Astellas' HB-MSC technology was limited to the purpose of the collaboration. (Ex. 39, IMSTEM-0002553-56 at -553.)

260. Defendants were informed that they must keep Astellas' HB-MSC technology confidential. (Ex. 25, IMSTEM-0004606-07 at -606-607.)

261. The promising results for Astellas' HB-MSCs in the preclinical multiple sclerosis model provided the first evidence of the clinical potential for these cells. (Ex. AC, IMSTEM-0002267-68.)

262. Defendants began efforts to commercially exploit Astellas' HB-MSC technology at least by September 2011. (Ex. AK, IMSTEM-0008577-578 (translation at AIRM00296707-740).)

263. Defendants began forming their own company based on Astellas' HB-MSC method and preclinical data as early as March 2012. (Ex. GL, IMSTEM-0040473-91.)

264. Defendants' company, ImStem, was incorporated on June 1, 2012. (Ex. 18, IMSTEM-0040593-601.)

265. Defendants' company relied on the use of Astellas' HB-MSCs to treat autoimmune diseases as a basis for its formation. (Ex. GL, IMSTEM-0040473-91 at -479.)

266. Defendants identified that Astellas' predecessor was expected to be a direct competitor for their newly formed company in ESC-derived MSCs. (Ex. 19, IMSTEM-0040434-53 at -444-45.)

267. Defendants relied on its patent filed in July 2012 on Astellas' HB-MSC technology to solicit investments. (Ex. AJ, IMSTEM-0023976-009 at -976.)

268. Astellas' patent application was published on June 6, 2013. (Ex. 3, AIRM0029661-46.)

269. The publication of Astellas' patent application was the first time that some of the confidential information about Astellas' HB-MSCs was publicly disclosed. (*see* Dkt. 129-22 at p. 20, Bell Rpt. at ¶ 44; *see* Ex. 3, AIRM00296616-46; Kimbrel Dep. at 262:2-263:13.)

270. Prior to the publication of Astellas' patent application, Astellas expected to be in complete control of access to its HB-MSC technology. (Ex. 39, IMSTEM-0002553-556.)

271. Defendants used their access to Astellas' HB-MSC technology to form a direct competitor to Astellas in ESC-derived MSCs. (*See, e.g.*, Ex. 19, IMSTEM-0040434-53 at -440-45.)

272. Defendants used their access to Astellas' HB-MSC technology as a "short cut" to establish a direct competitor to Astellas. (Xu. Dep. Tr. at 80:10-13, 75:14-17.)

273. The commercial potential for ImStem's ESC-derived MSCs do not appear to be associated with any scientific advantages as compared to Astellas' HB-MSCs. (Wang Dep. Tr. at 254:19-20, 255:6-9.)

274. Only by misusing Astellas' HB-MSC technology were Defendants able to form a direct competitor to Astellas in this field.

275. The value of ImStem reflects the amount by which Defendants were unjustly enriched from the misuse of Astellas' HB-MSC technology.

276. On June 22, 2013, ImStem received three equity investments totaling $593,000. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

277. The $593,000 equity investment was received in exchange for 593,000 shares of ImStem. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

278. These 593,000 shares constituted 37% of the 1,603,000 ImStem shares outstanding.

279. Investments totaling $593,000 for a 37% stake in ImStem implies a total value of $1,603,000.

280. At the time confidential information about Astellas' confidential HB-MSC technology was published, Defendants were unjustly enriched by at least $1.6 million from their misuse of Astellas' HB-MSC technology.

281. Defendants continued to solicit and receive investments in ImStem through December 21, 2016. (Ex. BB, IMSTEM-0045841-916 at -850 (redacted version at Ex. BA).)

282. The last investment in ImStem occurred on December 21, 2016. (*Id.*)

283. On December 21, 2016, Defendants received $1,800,000 for 150,000 shares of ImStem. (*Id.*)

284. On December 21, 2016, there were 3,086,333 ImStem shares outstanding.

285. Defendants received the $1,800,000 investment for a 4.86% stake in ImStem.

286. As of December 21, 2016, ImStem had an implied value of over $37 million.

287. The entire $37 million implied value of ImStem in December 2016 is based on the misuse of Astellas' technology.

b. Astellas' Requested Rulings of Law on Astellas' Unjust Enrichment Claim

288. Unjust enrichment is defined as "retention of money or property of another against the fundamental principles of justice or equity and good conscience." *Santagate v. Tower*, 833 N.E.2d 171, 176 (Mass. App. Ct. 2005) (citation omitted). To succeed on a claim of unjust enrichment, a plaintiff must show "(1) a benefit conferred upon the defendant by the plaintiff; (2) an appreciation or knowledge by the defendant of the benefit; and (3) acceptance or retention by the defendant of the benefit under the circumstances would be inequitable without payment for its value." *MEEI II*, 552 F.3d at 57.; *see also Karter v. Pleasant View Gardens, Inc.*, 248 F. Supp. 3d 299, 310 (D. Mass. 2017) (To prevail on a claim for unjust enrichment, plaintiff must establish that: "(1) [defendants] knowingly received a benefit (2) at [her] expense (3) under circumstances that would make retention of that benefit unjust.").

289. Astellas' unjust enrichment claim sounds in contract.[11] The First Circuit has explained that "[u]njust enrichment provides an equitable stopgap for occasional inadequacies in contractual remedies at law by mandating that '[a] person who has been unjustly enriched at the expense of another is required to make restitution to the other.'" *MEEI I*, 412 F.3d at 233-34 (quoting *Fox v. F & J Gattozzi Corp.*, 672 N.E.2d 547, 552 (1996)). Under Massachusetts law, unjust enrichment may sound in contract or in tort. *TargetSmart Holdings, LLC v. GHP Advisors,*

[11] The Court's summary judgment decision stated that "Plaintiffs' amended complaint frames their unjust enrichment claim as a misappropriation of intellectual property," which is a tort subject to a three-year statute of limitation. (Dkt. 163 at 12.) The Court applied a three-year statute of limitations to Astellas' unjust enrichment claim for purposes of its analysis at summary judgment but did not reach an ultimate conclusion on whether the claim sounds in contract or tort. (*See id.*)

LLC, 366 F. Supp. 3d 195, 212 n.2 (D. Mass. 2019) (citing *Salamon v. Terra*, 477 N.E.2d 1029, 1031 (1985); *MEEI II*, 552 F.3d at 57). To determine whether unjust enrichment sounds in contract or tort, courts look to the "gist of the action" or the essential nature of the plaintiff's claim. *Palandjian v. Pahlavi*, 614 F. Supp. 1569, 1577 (D. Mass. 1985), on reconsideration, No. CIV.A. 83-2199-Y, 1986 WL 15640 (D. Mass. Feb. 24, 1986), aff'd, 808 F.2d 1513 (1st Cir. 1986). Where the essence of the claim is that defendants "have failed to do as they promised," the "gist of the action" is contractual. *Barber v. Fox*, 632 N.E.2d 1246, 1249 (1994). Massachusetts courts have consistently held that unjust enrichment claims based on failed promises sound in contract. *See, e.g., Shutzer v. S. Rothschild & Co.*, No. CIV.A. 05-11486-MLW, 2006 WL 2691692, at *5 (D. Mass. Sept. 19, 2006) (plaintiff conferred substantial benefit on defendants after led to believe he was performing under a contract); *Diviacchi v. Affinion Grp., Inc.*, No. CIV.A. 14-10283-IT, 2015 WL 3631605, at *11 (D. Mass. Mar. 11, 2015), report and recommendation adopted, No. 14-CV-10283-IT, 2015 WL 3633522 (D. Mass. June 4, 2015) (defendants unjustly enriched by fees not authorized by plaintiff's membership); *Barber*, 632 N.E.2d at 1249 (fraud and breach of fiduciary duty for failure to convey land as promised).

290. Defendants admitted in their summary judgment briefing that "the breach of contract claim is . . . an ancillary basis for Plaintiffs' unjust enrichment claim." (Dkt. 135 at 15 n.18.) Indeed, the misappropriation of intellectual property that Astellas alleged in its unjust enrichment claim stemmed from Defendants' failure to live up to the confidentiality and limited use terms they specifically agreed to. *See Palandjian*, 614 F. Supp. at 1577-78 (holding that unjust enrichment resting in part on conversion but also to recover promised payment sounded in contract). Further, Defendants themselves repeatedly argued that there was no contract in this case based on their allegation that certain formal contractual terms were not met. Yet, Defendants do

not dispute that the parties discussed the need to keep materials confidential and limitations on use throughout the collaboration. Thus, Astellas' unjust enrichment claim is an "equitable stopgap for occasional inadequacies in contractual remedies." *See MEEI* I at 233-34. Thus, Astellas' claim is grounded primarily in contract, not tort.

291. Misuse of confidential information resulting from false promises can support unjust enrichment. *MEEI I* at 38. Under Massachusetts law, "[a] constructive trust is . . . imposed to avoid the unjust enrichment of one party at the expense of the other where 'information confidentially given or acquired was used to the advantage of the recipient at the expense of the one who disclosed the information.'" *Id.* (quoting *Mass Cash Register, Inc. v. Comtrex Sys. Corp.*, 901 F. Supp. 404, 423 (D. Mass. 1995)).

292. Defendants obtained substantial improper benefits at Astellas' expense by repeatedly furnishing false promises to Astellas. As discussed above for unfair trade practices, Defendants admitted that they had a general understanding of confidentiality underlying an academic collaboration like the one at issue. When Astellas reminded Defendants several times that the cells, methods, and data Astellas shared were confidential and could only be used for the limited purposes of the collaboration, Defendants repeatedly promised to keep confidential and not to misuse the materials Astellas shared. Yet Defendants went behind Astellas' back to include Astellas' confidential information in patent filings, grant applications, business plans, and investor presentations, and to rely on Astellas' technology to jump start their T-MSC work.

293. The Court has already found in summary judgment that "Defendants admit that Plaintiffs shared their protocol prior to it becoming public and that the protocol appears in Defendants' '551 patent." (Dkt. 163 at 8.)

294. Defendants benefitted by co-opting Astellas' confidential information, given solely for use in the collaboration, to obtain patents, grant funding, establish a competing business with multiple rounds of million-dollar investments, and to jump start their T-MSC work. Defendants claimed Astellas' technology as their own in their provisional applications and the '551 patent (and patents in the same family that Defendants have sought and continue to seek); relied on Astellas' method and data in several grant applications (including an award of over $1 million from the state of Connecticut); promoted themselves using Astellas' technology to solicit investors via business plans and presentations to form and then grow ImStem; and took information Astellas shared for use in the collaboration as a "shortcut" to develop T-MSCs.

295. Defendants were and continue to be aware of these benefits. Defendants intentionally filed applications for the '551 patent in order to use it as an "attack patent" to "prevent [Astellas] from using their technology to go to clinic and develop product" and to "ask for royalty from [Astellas] is they have successfully marketing [sic] their product." While maintaining an apparently amicable and collaborative relationship with Astellas, Defendants simultaneously monitored Astellas' patent filings and called Astellas a "major competitor" while discussing business plans for forming ImStem and filing applications for the '551 patent. Likewise, Defendants appreciated the benefit of Astellas' technology enough to incorporate it into their grant applications and financial solicitations. Defendants also continued to cite to Astellas' technology in grant application materials, including their 2016 grant progress report to the state of Connecticut. Defendants repeatedly claimed Astellas' technology as their own by submitting a sworn declaration the USPTO in 2017, and by continuing to file patent applications claiming Astellas' technology, including one that issued in 2020. Even today, Defendants still list the '551 patent on ImStem's website to promote their T-MSC product.

296. The circumstances of the collaboration make it inequitable for Defendants to retain these benefits without paying Astellas for their value. Defendants repeatedly supplied false promises to keep Astellas' technology confidential and to only use it for the purposes of the collaboration to induce Astellas to rely upon an apparent agreement between the parties to continue to share its confidential information to further what Defendants portrayed to be a mutual beneficial partnership. Yet Defendants did the exact opposite of their promises at Astellas' expense—they took Astellas' technology and put it into patents, grants, and commercial documents for Defendants' sole benefit. They also schemed to seek a royalty from Astellas and block Astellas in the market with their "attack" patent. Further, Defendants formed ImStem, a company to compete with Astellas based on Astellas' technology, without telling Astellas, and, at times, plotted to delay work for Astellas for the benefit of ImStem. While enjoying these benefits, Defendants not only took advantage of Astellas' time and money misused in furthering a disguised collaboration and performing according to the parties' agreement, but also granted themselves a free license and "shortcut" to use Astellas' intellectual property to grow their own business, without compensating Astellas for the value that it would otherwise have charged a competitor to use the technology.

297. The value of the benefit to Defendants can be determined based on the implied value of the investments and the price per share assigned to each. Astellas should also be granted equitable relief in the form of return all intellectual property rights that contain its MSC technology, including all patents and applications Defendants have filed, worldwide, that contain Astellas' MSC technology.

3. Conversion

a. Astellas' Proposed Findings of Fact on Astellas' Conversion Claim

298. Astellas incorporates its proposed findings of fact from Section II.A.1.a (¶¶ 190 - 244) here as if restated in full.

(1) Monetary damage to Astellas due to Defendants' conversion

299. Before they began collaborating with Astellas in July 2010, Defendants had no experience making MSCs from ESCs. (Wang Dep. Tr. at 282:23-285:4.)

300. Defendants' access to Astellas' HB-MSC technology was limited to the purpose of the collaboration. (Ex. 39, IMSTEM-0002553-56 at -553.)

301. Defendants were informed that they must keep Astellas' HB-MSC technology confidential. (Ex. 25, IMSTEM-0004606-07 at -606-07.)

302. Defendants began efforts to commercially exploit Astellas' HB-MSC technology at least by September 2011. (Ex. AK, IMSTEM-0008577-578 (translation at AIRM00296707-740).)

303. Defendants began forming their own company based on Astellas' HB-MSC method and preclinical data as early as March 2012. (Ex. GL, IMSTEM-0040473-91.)

304. Defendants' company, ImStem, was incorporated on June 1, 2012. (Ex. 18, IMSTEM-0040593-601.)

305. Defendants' company relied on the use of Astellas' HB-MSCs to treat autoimmune diseases as a basis for its formation. (Ex. GL, IMSTEM-0040473-91 at -479.)

306. Defendants identified that Astellas' predecessor was expected to be a direct competitor for their newly formed company in ESC-derived MSCs. (Ex. 19, IMSTEM-0040434-53 at -444-45.)

307. Defendants relied on its patent filed in July 2012 on Astellas' HB-MSC technology to solicit investments. (Ex. AJ, IMSTEM-0023976-009 at -976.)

308. Astellas' patent application was published on June 6, 2013. (Ex. 3, AIRM00296616-46.)

309. The publication of Astellas' patent application was the first time that some of the confidential information about Astellas' HB-MSCs was publicly disclosed. (*see* Dkt. 129-22 at p. 20, Bell Rpt. at ¶ 44; *see* Ex. 3, AIRM00296616-46; Kimbrel Dep. at 262:2-263:13.)

310. Prior to the publication of Astellas' patent application, Astellas expected to be in complete control of access to its HB-MSC technology. (Ex. 39, IMSTEM-0002553-56.)

311. Defendants used their access to Astellas' HB-MSC technology to form a direct competitor to Astellas in ESC-derived MSCs. (*See, e.g.*, Ex. 19, IMSTEM-0040434-53 at -440-45.)

312. Defendants used their access to Astellas' HB-MSC technology as a "short cut" to establish a direct competitor to Astellas. (Xu. Dep. Tr. at 75:14-17, 80:10-13.)

313. The commercial potential for ImStem's ESC-derived MSCs do not appear to be associated with any scientific advantages as compared to Astellas' HB-MSCs. (Wang Dep. Tr. at 254:19-20, 255:6-9.)

314. But-for Defendants misuse of their access to Astellas' HB-MSC technology, Astellas would have been the only commercial entity in the market for ESC-derived MSCs based on their technology. (*see* Dkt. 129-22 at p. 19, Bell Rpt. at ¶ 43; Bell Dep. Tr. at 147:16-148:9.)

315. The value of ImStem in June 2013 reflects the amount by which Astellas was damaged from Defendants' conversion of Astellas' confidential HB-MSC technology because it

represents Defendants' unauthorized capture of the value of the market for Astellas' HB-MSC technology.

316. On June 22, 2013, ImStem received three equity investments totaling $593,000. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

317. The $593,000 equity investments were received in exchange for 593,000 shares of ImStem. (Ex. BB, IMSTEM-0045841-916 (redacted version at Ex. BA).)

318. These 593,000 shares constituted 37% of the 1,603,000 ImStem shares outstanding.

319. Investments totaling $593,000 for a 37% stake in ImStem implies a total value of $1,603,000.

320. Astellas was damaged by at least $1.6 million as a result of Defendants' conversion of Astellas' HB-MSC technology.

b. Astellas' Requested Rulings of Law on Astellas' Conversion Claim

321. "A plaintiff asserting a conversion claim under Massachusetts law must show that: (1) the defendant intentionally and wrongfully exercised control or dominion over the personal property; (2) the plaintiff had an ownership or possessory interest in the property at the time of the alleged conversion; (3) the plaintiff was damaged by the defendant's conduct; and (4) if the defendant legitimately acquired possession of the property under a good-faith claim of right, the plaintiff's demand for its return was refused." *Evergreen Marine Corp. v. Six Consignments of Frozen Scallops*, 4 F.3d 90, 95 (1st Cir. 1993).

322. Conversion can occur if the defendant either did some positive wrongful act with the intention to appropriate the property to himself or to deprive the rightful owner of it, or destroyed the property. *Kelley v. LaForce*, 288 F.3d 1, 12 (1st Cir. 2002) (citing *Grande v. PFL Life Ins. Co.*, No. 9663, 2000 WL 1476676, at *4 (Mass. App. Div. Sept. 27, 2000)). "It is no

defense to conversion for defendant to claim that he acted in good faith, reasonably believing that he had a legal right to possession of the goods. *Id.* (citing *Kelly v. Dubrow*, No. 1313, 2001 WL 287490, at *3 (Mass. App. Div. Mar. 20, 2001)).

323. Defendants exercised ownership, control, or dominion over Astellas property by intentionally and wrongfully taking Astellas' method, cells, data and related know-how and claiming them as their own. By granting Astellas' motion for partial summary judgment to add Drs. Kimbrel and Lanza as co-inventors to the '551 patent, the Court effectively determined that Defendants exercised ownership, control, or dominion over Astellas' HB-MSC related property via their patent filings. (Dkt. 163 at 8-9.) The Court found that Defendants filed the '551 patent by claiming Drs. Kimbrel and Lanza's invention to the exclusion of these Astellas scientists. (*Id.*) In addition, Defendants exercised control over Astellas' property by claiming the novel HB-MSCs cells and method as their own in grant applications, commercial business plans, and investor documents. Defendants' conversion lasts from the time of the collaboration to the present. Defendants continue to claim ownership over Astellas' property by representing so to the state of Connecticut in 2016 and to the USPTO in 2017, receiving consecutively issued patents and filing additional applications based on the '551 patent, and promoting ImStem by listing the '551 patent on ImStem's website even today.

324. Defendants had no right to possess Astellas' property at the time due to Astellas' limitations on confidentiality and uses of its materials and Defendants' agreement thereto. It was Astellas' scientists who developed the method of deriving MSCs from hESC via an HB intermediate. The resulting cells, data, and intellectual property have always belonged to Astellas. Assured by Defendants' repeated promises, Astellas provided Defendants with its materials under the impression that these materials would only be used for the limited purposes of the collaboration

not for Defendants' patents and commercialization. Thus, Defendants have never legitimately acquired possession of Astellas' property.

325. Defendants cannot reasonably claim that they somehow acquired Astellas' technology in good faith. Whenever Astellas told them that the materials could not be disclosed and could only be used for the purposes of the collaboration, Defendants raised no objection, they only agreed. Defendants' continued wrongful possession of Astellas' property forced Astellas to seek judicial relief by filing this lawsuit. During litigation, Defendants never seriously "offered to add Drs. Kimbrel and Lanza as additional co-inventors to the '551 Patent" (Dkt. 71 at 3 n.6), necessitating the Court's intervention to accord Drs. Kimbrel and Lanza inventorship on the '551 patent by summary judgment.

326. Finally, Astellas was damaged in the amount of at least $1.6 million by Defendants' acts. Astellas spent considerable time and money in the form of employee and collaboration costs providing assistance, know-how, and money to ImStem to further the collaboration. Further, Astellas was damaged by having its intellectual property rights impaired, unwittingly assisting a competitor, and unknowingly being forced to grant a free license while losing the value that it would have charged a competitor for use of their technology. Astellas should also be granted equitable relief in the form of return all intellectual property rights that contain its MSC technology, including all patents and applications Defendants have filed, worldwide, that contain Astellas' MSC technology.

B. Defendants' Statute of Limitations Affirmative Defense

1. Astellas' Proposed Findings of Fact on Defendants' Statute of Limitations Affirmative Defense

327. Astellas incorporates its proposed findings of fact from Section II.A.1.a (¶¶ 190 - 244) here as if restated in full. Astellas proposes additional findings of fact as follows.

328. Astellas did not know and could not have known Defendants' insidious acts memorialized in their internal emails and confidential documents until discovery in this litigation. These acts include but are not limited to Defendants' original filing of the provisional applications that led to the '551 patent with an intent to "block" and "attack" Astellas from using *its own technology* and to "ask for royalty" in the event Astellas commercialized that technology. The acts further included disclosing Astellas' technology in an invention disclosure form to UConn to claim it as their own while hiding Astellas' original development of the HB-MSC method; treating Astellas as a major competitor in business proposals and patent search report; and misusing Astellas' technology in grant applications, business and investment solicitation, and to jump start their T-MSC work.

329. While Defendants filed the provisional applications that led to the '551 patent on July 12, 2012 and February 11, 2013, respectively (Ex. 3, AIRM00296616-646; Ex. 5, AIRM00296647-675), Astellas could not have found out either application until they published with the PCT application (WO 2014/011407, "2014 PCT publication") that claims priority to these provisional applications. (Ex. 37, AIRM00037251-387.)

330. Defendants' expert Dr. Zerhusen acknowledged that provisional applications at the time of filing are confidential and unknowable outside the patent office. (*See* Dkt. 143-16 at pp. 3-4, Expert Rpt. of Dr. Bryan Zerhusen ¶¶ 9-10.) Dr. Zerhusen stated in his report that "[d]ue to the confidential manner in which U.S. provisional patent applications are maintained, the provisional patent application is not accessible to the public until such time as a corresponding U.S. nonprovisional patent application or an International Patent Application is published, which occurs around 18 months after the earliest priority date (i.e., earliest provisional filing date)." (*Id.* at ¶ 9.) Dr. Zerhusen clarified in his deposition that "a provisional patent application is not publicly

accessible unless a nonprovisional claiming priority or incorporating by reference claiming priority to that provisional publishes." (Zerhusen Dep. 27:2-13, *see also* 27:14-29:3.)

331. The 2014 PCT publication published on January 16, 2014. (Ex. 37, AIRM00037251-387.) The 2014 PCT publication has similar disclosure as the '551 patent but does not include the issued claims of the '551 patent. (*See id.*)

332. On February 4, 2014, Astellas first became aware of the 2014 PCT publication. (Dkt. 113 at ¶ 62.)

333. Defendants have alleged that in May 2013, Astellas learned that Drs. Wang and Xu had formed ImStem. (*See* Dkt. 135 at 3.) However, Astellas did not know what particular stem cell technology ImStem was formed around at the time it was formed. (*See* Lanza Dep. 279:19-281:16.)

334. Moreover, during the course of the collaboration, Defendants intentionally concealed information about ImStem from Astellas. (*See* Ex. 20, IMSTEM-0031133-134 (upon Astellas' request for EAE experiments in August 2013, Dr. Wang stating to Mr. Men that "I will keep this under UConn for now and delay them a couple of months[,] so there is no interaction between ImStem and act [sic] so far" while telling Dr. Kimbrel that they could not start the experiment until October for various reasons).)

335. In June 2014, Astellas believed that Defendants could be pursuing T-MSCs, which Astellas could not have known were created using a jump start from Astellas' technology. (*See* Ex. OG, AIRM00097111-713 at AIRM00097111 ("IMStem has recently developed a methodology for generating MSCs through an alternative route (trophoblast-derived MSC). They have not published anything on the MSCs made by this new method, but if they are equivalent to the hemangioblast-derived MSCs than [sic] IMStem may have a manufacture process that is

outside the scope of our method of manufacture claims to the extent our claims require hemangioblast intermediates.").)

336. Indeed, Defendants have alleged in their interrogatory responses that "ImStem was founded upon and has pursued only its so-called 'T-MSC' technology – using a trophoblast as an intermediary, not a hemangioblast" and that T-MSCs "are beyond the scope of this litigation." (Ex. MJ, Defs. Xiaofang Wang and ImStem's Resp. to Astellas' Second Set of Interrog. (Nos. 22-30) at 9, 11; Ex. MG, Defendant Ren-He Xu's Resp. to Astellas' Second Set of Interrog. (Nos. 22-30) at 9, 11.)

337. On June 27, 2013, Defendants filed U.S. Patent Application No. 14/413,290 ("the '290 application), which is a national stage application of the 2014 PCT publication and published on July 23, 2015. (*See* Ex. A, AIRM00290341-411 at AIRM00290341.)

338. On July 21, 2017, Defendants filed U.S. Patent Application No. 15/656,473 ("the '473 application") as a child application of the '290 application that issued as the '551 patent. (Ex. MK.)

339. The '551 patent issued on August 29, 2017. (*See* Ex. A, AIRM00290341-411 at AIRM00290341; Attach. A to Pretrial Memo. at Stip. Fact No. 26.)

340. Astellas filed suit on November 13, 2017. (Dkt. 1.)

341. On January 17, 2020, Defendants filed U.S. Patent Application No. 16/745,944 as another child application of the '290 application that issued as the '551 patent.

342. On February 11, 2020, the '473 application issued as U.S. Patent No. 10,557,122 ("the '122 patent") with claims similar to those of the '551 patent. (*See* Ex. MK; Attach. A to Pretrial Memo. at Stip. Fact No. 38.)

2. Astellas' Requested Rulings of Law on Defendants' Statute of Limitations Affirmative Defense

343. Under Massachusetts law, "actions of tort . . . shall be commenced only within three years next after the cause of action accrues." Mass. Gen. Laws Ann. ch. 260, § 2A. Massachusetts courts applies this three-year statute of limitations to the tort of conversion. *Patsos v. First Albany Corp.*, 741 N.E.2d 841, 846 n.6 (Mass. 2001).

344. Claims arising under Chapter 93A "shall be commenced only within four years next after the cause of action accrues." Mass. Gen. Laws Ann. ch. 260, § 5A; *see Latson v. Plaza Home Mortg., Inc.*, 708 F.3d 324, 326 (1st Cir. 2013) ("The limitations period for chapter 93A actions is four years from injury.").

345. Unjust enrichment, a claim sounding in equity, can be subject to a three-year statute of limitations if the claim arises from a tort, or a six-year statute of limitations if the claim arises from a contractual dispute. *See Epstein v. C.R. Bard, Inc.*, No. 03-12297-RWZ, 2004 WL 1598912, at *3 (D. Mass. July 19, 2004) (citing *Desmond v. Moffie*, 375 F.2d 742, 743 (1st Cir. 1967)).

346. A cause of action for tort accrues "when a plaintiff discovers, or any earlier date when she should reasonably have discovered, that she has been harmed or may have been harmed by the defendant's conduct." *Bowen v. Eli Lilly & Co.*, 557 N.E.2d 739, 741 (Mass. 1990); *see Sheedy v. Deutsche Bank Nat'l Tr. Co.* (*In re Sheedy*), 801 F.3d 12, 20 (1st Cir. 2015) (citing *Bowen*). The "discovery rule" is also applicable in a Chapter 93A action. *Monteferrante v. Williams-Sonoma, Inc.*, 241 F. Supp. 3d 264, 271 (D. Mass. 2017) (citing *Cambridge Plating Co. v. NAPCO, Inc.*, 991 F.2d 21, 25 (1st Cir. 1993)).

> The test for whether a plaintiff should have discovered necessary facts is an objective one. We look first to whether sufficient facts were available to provoke a reasonable person in the plaintiff's circumstances to inquire or investigate further. 'A claim does not accrue when a person has a mere hunch, hint, suspicion, or rumor

> of a claim, but such suspicions do give rise to a duty to inquire into the possible existence of a claim in the exercise of due diligence.' Once a duty to inquire is established, the plaintiff is charged with the knowledge of what he or she would have uncovered through a reasonably diligent investigation. The next question is whether the plaintiff, if armed with the results of that investigation, would know enough to permit a reasonable person to believe that she had been injured and that there is a causal connection between the [defendant] and her injury. Definitive knowledge is not necessary.

McIntyre v. United States, 367 F.3d 38, 52 (1st Cir. 2004) (internal citations omitted) (quoting *Kronisch v. United States*, 150 F.3d 112, 121 (2d Cir. 1998)).

347. As discussed above in Section II.A.1.a (¶¶ 190 - 244, incorporated here as if restated in full), Astellas' state-law claims are based not only on Defendants' filing patents applications claiming Astellas' technology as their own, but also on many other insidious activities, including Defendants' misuses of Astellas' technology to found ImStem, apply for grants, solicit business and investments, and jump start their T-MSC work. Defendants' bad acts occurred throughout the limitations periods from November 13 in 2011 (unjust enrichment, which sounds in contract), 2013 (Chapter 93A), and 2014 (conversion) until today, with Defendants concealing numerous acts until discovery of this litigation.

a. Astellas' conversion claim is timely

348. First, the earliest possible date Astellas received information that hinted at *any* of Defendants' wrongful acts is February 4, 2014, when Astellas became aware of the 2014 PCT publication that has a similar disclosure to the '551 patent. This date is well within the statute of limitation periods for Astellas' unjust enrichment and Chapter 93A claims, and thus these state-law claims are timely.

349. Astellas could not have discovered Defendants' provisional applications when they were filed on June 12, 2012 and February 11, 2013, respectively. As Defendants' expert acknowledged, the USPTO keeps provisional applications confidential at the time of filing, and

they remain confidential until applicants take further action, such as by filing a Patent Cooperation Treaty ("PCT") application that claims priority to it (which publishes 18 months after the priority date), or by incorporating it into another published application.

350. At best, the 2014 PCT publication only hinted—at most—at one of Defendants' bad acts that form the basis of Astellas' state-law claims.

351. Defendants did not actually obtain claims in the United States until the issuance of the '551 patent on August 29, 2017.

352. Moreover, Defendants majorly amended their pending claims in a preliminary amendment filed January 7, 2015 to claim Astellas' HB-MSC method. (Ex. 8, AIRM00293495 at AIRM00293644-650.) The originally proposed independent claim 1 (which is claim 1 in Defendants' published PCT application, *see id*. at AIRM00293604) recited "[a] method of selecting clinical grade hES-MSCs for treating autoimmune disease." Defendants deleted this method in the preliminary amendment, replacing it with Astellas' HB-MSC method: (additions underlined, deletions ~~struckthrough~~):

1. (Currently Amended) A method for producing human embryonic stem cell-derived mesenchymal stem cells, comprising:

a. culturing human embryonic stem cells with serum free media with or without GSK3 inhibitors;

b. culturing human embryonic stem cells in serum-free media comprising vascular endothelial growth and bone morphogenic protein 4 (BMP4) in an amount sufficient to induce differentiation into embryoid bodies;

c. adding at least one growth factor to the culture, wherein the growth factor is in an amount sufficient to expand human hemangio-colony forming cells;

d. disaggregating the hemangio-colony forming cells into single cells; and

e. culturing the single cells in media containing serum, KOSR or other serum-free medium in an amount sufficient to induce differentiation of the single cells into mesenchymal stem cells;

wherein at least about 90% of the mesenchymal stem cells express CD73 ~~of selecting clinical grade hES-MSC for treating autoimmune diseases~~, said MSC having the following characteristics: (i) contain >95% of cells expressing group-1 markers; (ii) contain >80% of cells

(Ex. 8 at AIRM00293646.) Following a restriction requirement, Defendants then elected, on May 26, 2016, to pursue claims "drawn to methods for producing human embryonic stem cell derived mesenchymal stem cells" (Group I). (Ex. 8 at AIRM00293871-873.) In the first office action, which issued on July 28, 2016, the examiner rejected Defendants' claims as anticipated by Astellas' PCT application. ((Ex. 8 at AIRM00295646-656, -651.) All of this prosecution activity, which focused Defendants' claims further and further towards Astellas' HB-MSC technology, all occurred well within the statute of limitation periods for Astellas' unjust enrichment, Chapter 93A, and conversion claims.

353. "A claim does not accrue when a person has a mere hunch, hint, suspicion, or rumor of a claim." *SiOnyx, LLC v. Hamamatsu Photonics K.K.*, 332 F. Supp. 3d 446, 467 (D. Mass. 2018). "The Massachusetts court does not equate suspicion with knowledge, but is explicit in

requiring actual knowledge, or, as an equivalent, full means of detecting the fraud." *MEEI I*, 412 F.3d at 240. Although "[t]he plaintiff need not know the full extent of the injury before the statute starts to run," the First Circuit has clarified that the limitations period does not start if the plaintiff does not know "the full extent of its claim."[12] *Id.* at 241.

354. Nothing, including the 2014 PCT publication, would have informed Astellas that Defendants 1) founded ImStem on intellectual property misappropriated from Astellas, 2) relied on the misappropriated information to seek grants or investments, or 3) derived their T-MSC work from Astellas' HB-MSC technology.

355. Indeed, Astellas could not have discovered the full extent of its state-law claims in 2014.

356. In *Bank of Am., N.A. v. Barnes Hill LLC*, No. 16-CV-11583-DJC, 2019 WL 2085996, at *5 (D. Mass. May 13, 2019), the Court found Chase's counterclaim was not time-barred because, even if Chase knew or should have known the missing discharge of mortgage, it could not have discovered that Bank of America's internal missteps caused Chase's injury.

357. Similarly, Astellas could not have discovered Defendants' internal use of Astellas' HB-MSC technology to found ImStem, jump start their T-MSCs work, and solicit investors and grant money in 2014. "[A] plaintiff must be able to decide when the harms it has sustained require bringing suit, and no defendant should be able to immunize itself from later, potentially graver claims, by openly engaging in prior, similar offenses that the future plaintiff does not believe

[12] In their summary judgment reply brief, Defendants cited an old case *Olsen v. Bell Tel. Labs., Inc.*, 445 N.E.2d 609, 612 (1983) for the statement that "[i]f knowledge of the extent of injury were to control the accrual of a cause of action, the fixed time period of statutes of limitations effectively would be destroyed." (Dkt. 161 at 5.) However, the First Circuit has addressed a more recent case (*Bowen*) citing *Olsen*, and found that the district court incorrectly expanded the statement about "the full extent of the injury" to find that the plaintiff need not know "the full extent of its claim." *MEEI I*, 412 F.3d at 241.

warrant bringing suit." *MEEI I*, 412 F.3d at 241; *see also Hohri v. United States*, 847 F.2d 779, 784 n.6 (Fed. Cir. 1988) ("Forcing claimants to file a suit which may be subject to Rule 11 sanctions [or is likely to be dismissed on the pleadings] to beat a statute of limitations defense is not sound judicial policy.") (brackets in original).

358. *MEEI I* and *Tracerlab, Inc. v. Indus. Nucleonics Corp.*, 313 F.2d 97 (1st Cir. 1963) are instructive. In both cases, the plaintiffs knew that the defendants possessed their trade secrets and were "well aware from the very outset that [the defendants] had gone into the [same] field and were producing a competitive product." *MEEI I*, 412 F.3d at 240; *Tracerlab*, 313 F.2d at 99-100. The First Circuit found this "far different" from having knowledge that the defendants had misappropriated and used the same trade secrets underlying the cause of action. *Id.* The plaintiffs had even sent a letter (*MEEI I*) or formed an "opinion" (*Tracerlab*) that the defendants may have misappropriated trade secrets, yet the court found no "precise accusation" of any "particular instances of misappropriation" (*MEEI I*) or knowledge of any "specific, tangible or concrete facts" of the misuse (*Tracerlab*). *Id.* The court also noted that discovering the defendants' behind-closed-doors activities would be difficult. *Id.*

359. Even assuming that Defendants' 2014 PCT publication was sufficient to trigger an inquiry, Astellas conducted a diligent investigation only to conclude in June 2014 that Defendants could be pursuing T-MSCs, which Astellas could not have known were created using a jump start from Astellas' technology.

360. Further, even if Astellas learned about the existence of ImStem in 2013, it could not have known at the time that Defendants formed ImStem based on Astellas' technology, as Defendants actively concealed information about ImStem from Astellas.

361. Astellas' conclusion about ImStem's T-MSC focus was reasonable and consistent with Defendants' own assertions in their interrogatory responses that "ImStem was founded upon and has pursued only its so-called 'T-MSC' technology–using a trophoblast as an intermediary, not a hemangioblast" and T-MSCs "are beyond the scope of this litigation." *See UniRAM Tech., Inc. v. Taiwan Semiconductor Mfg. Co.*, 617 F. Supp. 2d 938, 947-48 (N.D. Cal. 2007) (finding that plaintiff "was free to believe that [defendant] was developing a similar product independently and that [plaintiff] was not the victim of any wrongful conduct").

362. It was only much later that Astellas found out Defendants developed T-MSCs by relying on Astellas' HB-MSC technology.

363. A failure to uncover the cause of action despite exercising reasonable diligence is sufficient to toll the statute of limitations. *Cambridge Plating*, 991 F.2d at 27. Thus, even if the 2014 PCT publication or the existence of ImStem triggered a duty to investigate, a reasonably diligent investigation would not have uncovered the full extent of Astellas' state-law claims. As such, Astellas' state-law claims are timely.

364. Moreover, Astellas' conversion claim is timely filed after the '551 patent issued in 2017.

365. In misappropriation-based torts, the statute of limitations does not run until the property is destroyed or converted. *Prescott v. Morton Int'l, Inc.*, 769 F. Supp. 404, 407 (D. Mass. 1990). Proprietary information disclosed in an application is not totally and completely destroyed until the issuance of a patent, which gives the public notice that the patentee claims exclusive

ownership of the information and appropriates the idea for the patentee's exclusive use. *Id.* at 407, 409.[13]

366. Defendants' '551 patent did not issue until August 29, 2017, and Astellas promptly sued less than three months later.

367. Second, Defendants' fraudulent concealment of their bad acts tolls the limitation periods.

368. Even assuming Astellas had sufficient notice and could have uncovered the full extent of its state-law claims in February 2014 (it could not), Defendants' failure to disclose their wrongful uses of Astellas' technology tolls the statutes of limitations.

369. Mass. Gen. Laws Ann. ch. 260, § 12 tolls the limitations period when a defendant fraudulently conceals the basis for a cause of action. Where a fiduciary relationship exists, a defendant fraudulently conceals when it fails to affirmatively and adequately disclose facts that would give rise to a claim. *Demoulas v. Demoulas Super Markets, Inc.*, 677 N.E.2d 159 (Mass. App. Ct. 1997).

370. Fiduciary duties exist between parties where, e.g., "the contract or transaction was intrinsically fiduciary and, therefore, required perfect good faith." *MEEI I*, 412 F.3d at 242. Even in the absence of an express contract, breach of the duty of disclosure substitutes for the active fraud normally required to constitute fraudulent concealment under § 12 where the fiduciary

[13] Regardless of whether an application publishes, *Prescott* stands for the policy that obtaining issued patent rights based on confidential information included in the application represents a finality and clarity of intention to claim the converted information beyond merely filing an application. This is consistent with the Federal Circuit's interpretation of 35 U.S.C. § 256 to require an issued patent, not merely a filed application, for filing a correction-of-inventorship claim. *Pei-Herng Hor v. Ching-Wu Chu*, 699 F.3d 1331, 1335 (Fed. Cir. 2012).

relationship arises from one party's repose of trust and confidence in another. *Burns v. Mass. Inst. of Tech.*, 394 F.2d 416, 419 (1st Cir. 1968).

371. Under Massachusetts law, failing to learn of a wrongful act due to a fiduciary's failure to disclose does not trigger any duty to exercise due diligence. *MEEI I*, 412 F.3d at 242. Hence, once fraudulent concealment is established, the limitations period is tolled until the plaintiff has *actual* knowledge of the operative facts. *Id.*

372. Whether a fiduciary relationship exists depends on whether the parties' relationship was one of trust and confidence; whether the plaintiff relied upon the defendants' specialized knowledge or judgment; whether the defendants were aware of the plaintiff's reliance upon them; and whether the defendants abused the plaintiff's trust and confidence to the plaintiff's disadvantage. *Stark v. Advanced Magnetics, Inc.*, 736 N.E.2d 434, 442 (2000).

373. Defendants owed Astellas a fiduciary duty.

374. Massachusetts courts recognize that scientific collaborations involving trusted confidential information give rise to a duty of disclosure. *See, e.g.*, *MEEI I*, 412 F.3d at 242 (by entering into a joint research relationship, MEEI put its valuable trade secrets in QLT's hands, requiring full disclosure of any misappropriation of those secrets); *Stark v. Advanced Magnetics, Inc.*, 29 F.3d 1570, 1578 (Fed. Cir. 1994) (a relationship of trust can be based on scientific collaboration over several years); *Stark*, 736 N.E.2d at 442-43 (same after refiled in state court); *Sentinel Prod. Corp. v. Mobile Chem. Co.*, No. 98-11782-PBS, 2001 WL 92272, at *13 (D. Mass. Jan. 17, 2001) (jury could reasonably find the existence of a fiduciary relationship where defendant contracted for access to plaintiff's trade secrets).

375. Defendants' promises to keep Astellas' information confidential and to induce Astellas' trust over the years of collaboration established a fiduciary duty of disclosure.

376. Astellas' confidentiality emails and Defendants' repeated assurances manifest a confidential relationship between the parties. Even Dr. Xu admitted Defendants' confidential obligations based on the parties' academic collaboration. Relying on Defendants' agreement to abide by the promised confidentiality and use limitations, Astellas continued to share cells, data, and technical know-how as Defendants knowingly continued to request such materials. Yet, Defendants were disclosing the received materials and using them to file their own patents, start their own company, and plot against Astellas, while concealing these acts from Astellas. For example, Astellas could never have discovered until this litigation that on the same day Defendants agreed to Astellas' emailed terms for confidentiality, they were monitoring Astellas' patent filings, and identifying Astellas as a major competitor whom they hoped to block or coerce into paying royalties on their own technology. Thus, Defendants' acts tolled the limitations period until Astellas had actual knowledge of these acts, the full extent of which did not occur until after November 13, 2014.

377. Defendants not only failed to disclose but affirmatively concealed their wrongdoing.

378. For example, Defendants never informed Astellas that they had filed patents on Astellas' technology. Defendants also plotted to delay Astellas' experiments and to disguise ImStem under UConn. By reassuring Astellas that they would safeguard Astellas' confidential information and materials, Defendants fraudulently concealed their simultaneous wrongful uses of Astellas' technology in patent filings, grant applications, business solicitation, and to jump start their T-MSC work. It was not until after onset of this suit that Astellas discovered Defendants' true intention to "attack" and "prevent [Astellas] from using their technology to go to clinic and develop product." Defendants' egregiously fraudulent conduct thus tolls the limitations period.

379. Third, Defendants' continuing bad acts toll the limitation periods.

380. A continuing tort that tolls the statute of limitations arises not by continuing ill effects from an original tort but by continual unlawful acts. *Maslauskas v. United States*, 583 F. Supp. 349, 351 (D. Mass. 1984).

381. Even though Defendants' PCT patent filing became public in 2014, the First Circuit has rejected that "in a complex case of this nature—where trade secrets of varying importance are alleged to have been divulged over a period of years—that notice of one misappropriation can constitute sufficient notice to begin tolling the statute for all misappropriations." *MEEI I*, 412 F.3d at 240. A wronged party like Astellas "should not be prejudiced with regards to later torts committed against it, simply because a defendant started the clock running by committing similar acts at an earlier time." *Id.* at 241.

382. Defendants' unlawful misappropriations of Astellas' proprietary information continue to the present day.

383. For example, on January 12, 2017, Defendants falsely signed affidavits swearing they were the sole inventors of the subject matter in the '551 patent to overcome the Patent Office's rejection of their claims as anticipated by Astellas' work.

384. Defendants continued to apply for new patents on Astellas' HB-MSC technology without informing the Patent Office of either the existence of this litigation, or Astellas' ownership of the subject matter of the claims, or the Court's summary judgment ruling to add Drs. Kimbrel and Lanza as co-inventors to the '551 patent. Earlier this year, Defendants obtained another issued patent US 10,557,122 as a child application of the '551 patent, and filed yet another child application No. 16/745,944 in the same family, with similar claims and naming only Drs. Wang and Xu as inventors. *See Stark*, 29 F.3d at 1578 (additional patents issued less than three years

before suit facially avoided the period of limitations); *Prescott*, 769 F. Supp. at 408 (adopting majority rule of continuing tort that provides separate causes of action for continued application for and granting of a patent).

385. Defendants continued to enjoy grants funded on the basis of the misappropriated technology up to at least October 31, 2016.

386. Further, Defendants have received equity investments as recently as four transactions from November and December 2016. Even today, ImStem's website lists the '551 patent to promote ImStem's MSC technology.

387. On October 16, 2017, Defendant ImStem transferred the rights to a Chinese patent claiming priority to the '787 and '961 provisionals and to PCT Application No. PCT/US2013/048291, to which the '551 patent claims priority, to Chinese ImStem. (Ex. MJ, Resp. to Interrog. No. 28, Defs. Wang & ImStem's Resp. to Astellas' Second Set of Interrog. (July 16, 2019).)

388. Defendants' continuing tort thus tolls the limitations periods.

b. Astellas' unjust enrichment claim is timely

389. As discussed above in Section II.A.2.b (¶¶ 288- 297, incorporated here as if restated in full), Astellas' unjust enrichment claim sounds in contract and thus was timely filed within the six-year statute of limitations.

390. To the extent that the Court finds that this claim sounds in tort, it is nevertheless timely within the three-year statute of limitations as applied to torts for the same reasons stated above for conversion.

c. Astellas' Chapter 93A claim is timely

391. Again for the same reasons stated above for conversion, Astellas' Chapter 93A claim filed November 13, 2017, was timely filed in view of the undisputed four-year statute of

limitations applying to such actions. Astellas could not have known about the filing of a patent application or Defendants other bad acts until well after November 13, 2013.

C. Defendants' Unjust Enrichment Claim

392. Defendants have alleged that Astellas was unjustly enriched by including data from the EAE experiments they asked Dr. Wang to perform using Astellas' HB-MSCs to verify the immunotherapeutic properties of those HB-MSCs and other "various inventive ideas and additions they made the HB-MSC protocol" in the '358 provisional and '956 and '321 patents. (*See* Dkt. 91 at Countercl. ¶¶ 50-63.)

1. Astellas' Proposed Findings of Fact on Defendants' Unjust Enrichment Claim

a. Defendants Have Not Shown Retention of Any Benefit Would be Inequitable

393. As described *supra* in Section I.B. (¶¶ 149I.A.1.a(1)73 - 188 incorporated here as if restated in full), Defendants' alleged contributions to Astellas' '956 and '321 patents, at best, merely explain the state of the art and are not significant to the inventions claimed therein.

394. Defendants have presented no evidence that Astellas' retention of the benefits that Defendants alleged to have conferred on Astellas would be inequitable. As described *supra* in Section II.A.1.a (¶¶ 190 - 244, incorporated here as if restated in full), from the outset, the Parties agreed that Drs. Wang and Xu would verify the therapeutic efficacy of Astellas' HB-MSCs by testing them in the EAE mouse model in return for a jointly authored paper. Drs. Wang and Xu received the benefit that the Parties agreed to—Dr. Wang is the first author and Dr. Xu is the last author on the Parties' joint paper published in Stem Cell Reports in 2014. (Ex. 9, Wang, X., Kimbrel, E.A., Ijichi, K., Paul, D., Lazorchak, A.S., Chu, J., Kouris, N.A., Yavanian, G.J., Lu, S.-J., Pachter, J.S., Crocker, S.J., Lanza, R., & Xu, R.-H. (2014) Human ESC-derived MSCs

outperform bone marrow MSCs in the treatment of an EAE model of multiple sclerosis. *Stem Cell Reports*. 3:115-130.)

395. For academic researchers like Drs. Xu and Wang, publication of scientific articles is a substantial benefit as it is a key component used for determining promotions and evaluating grant applications.

396. Defendants' actions throughout the collaboration indicate that they knew the agreed-upon benefit to them would be the jointly-authored paper, not inclusion as inventors on Astellas' patents. Astellas repeatedly informed Drs. Wang and Xu that it was filing patent applications on its HB-MSC technology. (*See, e.g.*, (Ex. 39, IMSTEM-0002553-556 at IMSTEM-0002553 ("As we are a company and have not yet filed our patent for the MSC stuff, please DO NOT distribute the slides to anyone else. The data should only be used for your internal departmental presentations or Xu lab meetings. Please please do not use the data for any other purposes. This is very important for our viability as a company!"); Ex. 13, IMSTEM-0004720-721 at IMSTEM-0004721 (November 18, 2011 email from Dr. Kimbrel telling Defendants that "ACT is particularly interested in developing our MA09-MSCs as a therapeutic product" and, "[i]n fact, a patent application for our MSCs is already being drafted"); Xu Dep. at 110:1-9 (admitting that he saw that Astellas informed him it was drafting a patent on its HB-MSCs).)

b. Defendants' Unjust Enrichment Claim is Time Barred

397. Defendants were also aware of the subject matter of Astellas' HB-MSC patents, including the '358 provisional, at least as early as June 21, 2013, when Dr. Wang sent an ImStem employee copies of Astellas' '358 provisional and PCT publication (which published only days before, on June 6, 2013). (Ex. 49, IMSTEM-0022056-90 at IMSTEM-0022056, -141.)

398. Yet, despite being aware that Astellas was filing patent applications on its HB-MSC technology, and aware that Astellas included the data from the EAE pilot study (which was actually

performed at Yale, by Yale scientists) in the '358 provisional, Defendants did not raise any concerns about inventorship of Astellas' patents until January 10, 2018 in Dr. Wang and ImStem's first Answer and Counterclaims responding to Astellas' original Complaint. (Dkt. 20.)

399. Even then, Dr. Wang and ImStem only raised inventorship concerns as to Astellas' '956 patent. (*See* Dkt. 20.) Defendants did not move for leave to amend their counterclaims to add inventorship claims to add Dr. Xu to Astellas' '956 patent and Drs. Wang and Xu to Astellas' '321 patent until about 11 pm Eastern on July 22, 2019, the night before a Status Conference with the Court. (Dkts. 70, 71.) This was over a year after Defendants' own counsel admitted in March 2018 that Dr. Wang "had nothing to do with the 321 patent concerning the generation of the cells." (Ex. EY, LU-00000003-090 at -069-70 (67:18-68:3).)

400. On August 11, 2019, the Court denied Defendants' motion to amend their counterclaims to assert a claim to add Dr. Xu as an inventor on the '956 patent. (Dkt. 85 at 11.) The Court explained:

> There is no excuse for Dr. Xu's lack of diligence in asserting counterclaims related to the '956 Patent. Dr. Xu's co-defendants, ImStem and Dr. Wang, asserted a counterclaim seeking a correction of inventorship on the '956 Patent on January 10, 2018. [ECF No. 20]. Dr. Xu did not file his own answer until June 8, 2018, at which time he had been on notice of the Counterclaim Complaint for nearly six months. [ECF No. 33]. At the time of the filing of the proposed amended counterclaims, Dr. Xu had been aware of the Counterclaim Complaint for over eighteen months. This apparent indifference by Dr. Xu cannot be overcome by any geographic or language barriers that he or his counsel may face and precludes a finding of good cause.

(*Id.*)

401. Defendants were aware of Astellas' patent applications and the content thereof at least as early as June 21, 2013. At that time, Defendants could have uncovered the full extent of their unjust enrichment claim through a reasonable investigation.

c. Defendants Have Unclean Hands

402. Separately, as described *supra* in Section II.A.1.a (¶¶ 190 - 244) regarding Astellas' Unfair Trade Practices claim (and as incorporated in Astellas' unjust enrichment and conversion claims at ¶¶ 257 and 298, respectively), Defendants committed misconduct throughout the collaboration. This includes, for example, repeatedly promising to keep Astellas' HB-MSC technology confidential and only use it for the limited purposes of the collaboration, while all the while breaking those promises behind Astellas' back and exploiting Astellas' HB-MSC technology for their own gain.

d. Defendants Have Not Provided Evidence of the Value of the Alleged Benefit

403. Defendants have not provided the value, or a reasonable approximation thereof, for the benefit Defendants allegedly conferred on Astellas. The Court granted Astellas' motion for partial summary judgment on the issue of monetary damages for Defendants' unjust enrichment counterclaim, finding that "Defendants' failure to provide expert or other evidence in support of a specific restitution award precludes their ability to recover monetary damages based on unjust enrichment." (Dkt. 163 at 11.) The Court explained that "[s]hould Defendants succeed in their unjust enrichment counterclaim, they will be limited to equitable relief, excluding restitution or other monetary relief." (*Id.*)

404. Defendants refused to provide "the value of Defendants' alleged contribution to the subject matter of the '321 patent, including but not limited to any analysis, valuation, assessment or accounting thereof" as requested by Astellas' interrogatories. Instead, Defendants objected "to this interrogatory to the extent it seeks expert testimony or opinion" and stated only that Defendants "have not performed any analysis, valuation, assessment or accounting of the monetary value of Defendants' contributions to the subject matter of the '321 patent." (Ex. MI, Resp. to

Interrog. No. 35 at p. 10, Defs.' Resp. to Astellas' Third Set of Interrog. (Signed by Drs. Xu and Wang on Oct. 14 & 15, 2019, despite Certificate of Service attesting to service "on October 11, 2019").)

405. Defendants did not provide any expert opinion as to any "value of Defendants' alleged contribution to the subject matter of the '321 patent" or the '956 patent. Defendants' opening expert reports (which should have contained any such expert opinion) were served ***before*** Defendants served their interrogatory response objecting "to the extent it seeks expert testimony or opinion." (*Compare* Ex. MI, Defs.' Resp. to Astellas' Third Set of Interrog. (Signed by Drs. Xu and Wang on Oct. 14 & 15, 2019, despite Certificate of Service attesting to service "on October 11, 2019") *with* Dkt. 106 ("Expert disclosures pursuant to Fed. R. Civ. P. 26(a)(2) shall be served by October 4, 2019") (emphasis in original).)

406. In their opposition to Astellas' motion for summary judgment, Defendants pointed to paragraphs 65-89 of their expert's, Dr. Bunnell's, report for "illustrating how valuable the Defendants' contributions were." (Dkt. 152 at 16-17.) However, Defendants ignored that Dr. Bunnell expressly testified in his deposition that "I'm not addressing any of the state law claims in my report."

407. Defendants cannot produce any evidence regarding the value of their alleged contributions to the '956 and '321 patents at trial. The Court granted Astellas' motion *in limine* that Drs. Wang and Xu "may not testify as experts as to their opinion on the patents and inventive processes at issue."[14] (Dkt. 209.) Given that Defendants refused to answer Astellas' interrogatory asking them to describe value of Defendants' alleged contributions to Astellas' patents, that they

[14] Drs. Wang and Xu have also not produced any evidence—or even alleged—that they are qualified to opine on the value of any of their alleged contributions to Astellas' patents, even if they were permitted to provide expert testimony (which they are not).

"have not performed any analysis, valuation, assessment or accounting of the monetary value of Defendants' contributions to the subject matter of the '321 patent," and their failure to provide expert testimony on this point, Defendants cannot present evidence of the alleged total or gross amount, or a reasonable approximation of, Astellas' alleged gain.

2. Astellas' Requested Rulings of Law on Defendants' Unjust Enrichment Claim

408. Unjust enrichment is defined as "retention of money or property of another against the fundamental principles of justice or equity and good conscience." *Santagate*, 833 N.E.2d at 176 (citation omitted). To succeed on a claim of unjust enrichment, a plaintiff must show "(1) a benefit conferred upon the defendant by the plaintiff; (2) an appreciation or knowledge by the defendant of the benefit; and (3) acceptance or retention by the defendant of the benefit under the circumstances would be inequitable without payment for its value." *MEEI II*, 552 F.3d at 57.; *see also Karter*, 248 F. Supp. 3d at 310 (To prevail on a claim for unjust enrichment, plaintiff must establish that: "(1) [defendants] knowingly received a benefit (2) at [her] expense (3) under circumstances that would make retention of that benefit unjust.").

409. "The [Plaintiff's] burden was to prove by a preponderance of the evidence that [Defendant] was 'unjustly enriched by the acquisition of title to identifiable property at the expense of the [Plaintiff] or in violation of the [Plaintiff's] rights.' Included within this burden is the obligation of the [Plaintiff] to present evidence of the total or gross amount of the defendant's gain, or a reasonable approximation thereof." *Sacco v. Circosta*, No. 17-P251, 2018 Mass. App. Unpub. LEXIS 454, at *4 (Mass. App. Ct. 2018) (internal citations omitted) (quoting Restatement (Third) of Restitution and Unjust Enrichment § 55(1), at 296 (2011)); *see also Bonina v. Sheppard*, 78 N.E. 3d 128, 134 (Mass. App. Ct. 2017) ("Moreover, in the present case, neither the plaintiff nor the defendant presented evidence regarding other possible measures of unjust enrichment, such as

the increased value of the home resulting from the materials and the services. As such, the trial judge had no other reliable, measurable basis on which to calculate the award").

410. "A court has 'wide discretion to withhold punishment of behavior which it considers not to warrant so severe a sanction' under the equitable maxim that 'he who comes into equity must come with clean hands.'" *Singh v. Blue Cross & Blue Shield of Mass., Inc.*, 182 F. Supp. 2d 164, 177 (D. Mass. 2001), aff'd sub nom. *Singh v. Blue Cross/Blue Shield of Mass., Inc.* 308 F.3d 25 (1st Cir. 2002) (quoting *Norton Co. v. Carborundum Co.*, 530 F.2d 435, 442 (1st Cir. 1976)); *Texaco P.R., Inc. v. Dep't of Consumer Affairs,* 60 F.3d 867, 880 (1st Cir. 1995) ("It is old hat that a court called upon to do equity should always consider whether the petitioning party has acted in bad faith or with unclean hands").

411. "The doctrine of unclean hands applies only when the plaintiff's misconduct is 'directly related to the merits of the controversy between the parties.'" *Am. Freedom Def. Initiative v. Mass. Bay Transp. Auth.*, No. CIV.A. 14-10292-NMG, 2014 WL 1093138, at *3 (D. Mass. Mar. 17, 2014), aff'd 781 F.3d 571 (1st Cir. 2015) (quoting *Texaco P.R., Inc.*, 60 F.3d at 880).

412. "The misconduct need not be punishable as a crime or give rise to a civil claim so long as it can be said to 'transgress equitable standards of conduct.'" *Id.* (quoting *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 815 (1945)).

413. Unjust enrichment, a claim sounding in equity, can be subject to a three-year statute of limitations if the claim arises from a tort, or a six-year statute of limitations if the claim arises from a contractual dispute. *See Epstein*, 2004 WL 1598912, at *3 (citing *Desmond v. Moffie*, 375 F.2d 742, 743 (1st Cir. 1967)).

414. A cause of action for tort accrues "when a plaintiff discovers, or any earlier date when she should reasonably have discovered, that she has been harmed or may have been harmed

by the defendant's conduct." *Bowen*, 557 N.E.2d at 741; *In re Sheedy*, 801 F.3d at 20 (citing *Bowen*).

a. Defendants Have Not Shown Retention of Any Benefit Would be Inequitable

415. Defendants have failed to prove that Astellas was unjustly enriched by its actions. To the contrary, Astellas clearly set forth the scope of the parties' collaboration and the benefit—a jointly authored paper—that Defendants would receive in return for verifying the therapeutic efficacy of Astellas' HB-MSCs by testing them in the EAE mouse model. Defendants received that agreed-upon benefit and Astellas received the agreed-upon verification data. That Astellas included this verification data in its patents is not inequitable or unjust. It is the end result of the Parties' agreed-upon bargain.

416. This type of collaborative arrangement, where academics get a jointly-authored paper based on their testing of a company's proprietary technology, is consistent with the understanding of the scope of such collaborations in the industry. As such, it cannot be against the fundamental principles of justice or equity and good conscience.

b. Defendants' Unjust Enrichment Claim is Time Barred

417. Defendants' unjust enrichment claim is time barred. Defendants' unjust enrichment claim sounds in equity (indeed, Defendants are limited to only equitable remedies assuming they succeed on this claim) and thus is subject to a three year statute of limitations. *See Epstein*, 2004 WL 1598912, at *3 (citing *Desmond v. Moffie*, 375 F.2d 742, 743 (1st Cir. 1967)). As such, the statutory bar arose no later than January 1, 2015,[15] based on Defendants' Wang and ImStem's filing of their original Answer and Counterclaims.

[15] While Massachusetts law tolls the statute of limitations for certain tort claims raised as counterclaims, such tolling cannot result in an affirmative recovery for the counterclaim plaintiff

418. Defendants' unjust enrichment claim is based solely on the inclusion of Drs. Wang and Xu's alleged contributions in the '956 and '321 patents.[16] Astellas informed Defendants as early as November 2011 that it was filing patent applications on its HB-MSC technology.[17] Further, Defendants were monitoring Astellas' patent filings at least as early as April 2012, when Drs. Wang and Xu emailed among themselves about a patent search report monitoring patent filings by their "two major competitor[s]," one of which was ACT, Astellas' predecessor. And Defendants were aware of the subject matter of Astellas' HB-MSC patents, including the '358 provisional that contains the pilot EAE data which is one basis of Defendants' unjust enrichment claim, at least as early as June 21, 2013, when Dr. Wang sent an ImStem employee copies of Astellas' '358 provisional and PCT publication. Defendants should have discovered the extent of

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and only applies where monetary recovery is sought by the counterclaim defendant. *Howell v. Birnberg*, No. 92-2842-A, 1 Mass. L. Rep. 636, at *13 (Mass. Super. Ct. Feb. 10, 1994) ("A counterclaim under [G.L.c. 260,] 36, which goes only to the extent of the plaintiff's claim . . . corresponds to recoupment in pre-Rules practice. *Bernstein v. Gramercy Mills, Inc.*, 16 Mass. App. Ct. 403, 409, 452 N.E.2d 231 (1983). Recoupment served to reduce or extinguish the plaintiff's claim, but it ***could not result in an affirmative recovery*** for the defendant. *Bose Corp. v. Consumers Union of United States, Inc.*, 367 Mass. 424, 427-28, 326 N.E.2d 8 (1975). The statute clearly contemplates application ***only where monetary recovery is sought*** by the plaintiff.") (internal quotation marks omitted) (emphasis added). Further, the remedy for such tolled claims is limited to a set-off of the counterclaim defendants' damages. *Arthur D. Little Int'l v. Dooyang Corp.*, 928 F. Supp. 1189, 1204 (D. Mass. 1996) (answering the question of "whether the three-year statute of limitations [for the negligence claim] limits recovery" by determining that "[b]ecause this counterclaim arises out of the same transaction or occurrence as the claims in the complaint, ***it remains as a set-off to ADL's damages***") (emphasis added). Thus, tolling of the statute of limitations is not appropriate here where Defendants failed to produce any evidence of the monetary value of their unjust enrichment claim and, because of such failure, the Court granted summary judgment limiting Defendants to equitable relief, excluding restitution or other monetary relief, to the extent they are successful on their unjust enrichment claim.

[16] Defendants' unjust enrichment claim thus differs from Astellas' unjust enrichment claim, which includes Defendants' co-opting Astellas' confidential information, given solely for use in the collaboration, to obtain patents, grant funding, establish a competing business with multiple rounds of million-dollar investments, and to jump start their T-MSC work, despite promising to treat Astellas' technology as confidential and only use it for purposes of the collaboration.

[17] Thus, unlike Astellas, Defendants cannot rely on a theory of fraudulent concealment to toll the limitation period.

their unjust enrichment claim in 2013 when they first saw that Astellas included EAE data from the collaboration in its patent applications.

419. Defendants further should have discovered the extent of their unjust enrichment claim in 2014 when the application that issued as the '956 patent was published as U.S. Patent Application Publication No. US2014/0072537 on March 13, 2014. As evidenced by Defendants' earlier emails, they were monitoring Astellas' patent filings as Astellas was one of "two major competitors" and the collaboration had not yet ended, given that the Parties' joint paper had not yet published in Stem Cell Reports (on July 8, 2014).

c. Defendants' Unjust Enrichment Claim is Barred By The Doctrine of Unclean Hands

420. Even if Defendants met their burden to prove all elements of their unjust enrichment claim, Defendants' claim is barred by the doctrine of unclean hands.

421. As explained *supra* Section II.A.1. (¶¶ 190 - 256, incorporated here as if restated in full), Defendants committed unfair or deceptive acts by misappropriating Astellas' technology under the guise of an academic collaboration and misusing Astellas' technology for commercial gain. Defendants' unfair or deceptive acts more than meet the standard for unclean hands, given that they gave rise to Astellas' civil claim for Unfair Trade Practices under Chapter 93A. "The misconduct need not be punishable as a crime or give rise to a civil claim so long as it can be said to 'transgress equitable standards of conduct.'" *Am. Freedom Def. Initiative*, 2014 WL 1093138, at *3 (stating that "misconduct need not be punishable as a crime or give rise to a civil claim so long as it can be said to 'transgress equitable standards of conduct'") (quoting *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 815 (1945)).

422. As explained *supra* Section II.A.2 (¶¶ 257 - 297, incorporated here as if restated in full), Defendants were unjustly enriched by co-opting Astellas' confidential information, given

solely for use in the collaboration, to obtain patents, grant funding, establish a competing business with multiple rounds of million-dollar investments, and to jump start their T-MSC work, despite promising to treat Astellas' technology as confidential and only use it for purposes of the collaboration. Defendants' bad acts more than meet the standard for unclean hands, given that they give rise to Astellas' unjust enrichment claim. *Id.*

423. As explained *supra* Section II.A.3 (¶¶ 298 - 326, incorporated here as if restated in full), Defendants converted Astellas' property by exercising ownership, control, or dominion over Astellas property by intentionally and wrongfully taking Astellas' method, cells, data and related know-how and claiming them as their own. Defendants' bad acts in intentionally and wrongfully taking Astellas' technology and claiming it as their own more than meet the standard for unclean hands, given that they give rise to Astellas' conversion claim. *Id.*

d. Defendants Have Not Provided Evidence of the Value of the Alleged Benefit

424. Separately, Defendants have failed to meet their burden to make out an unjust enrichment claim because they have failed to provide any evidence of the value, or a reasonable approximation thereof, of their alleged contributions to Astellas' '956 or '321 patents. The sole evidence Defendants' pointed to in their summary judgment briefing on this point was a series of paragraphs from the expert report of Dr. Bunnell, who at his deposition testified that "I'm not addressing any of the state law claims in my report."

425. Further, Defendants cannot offer any testimony—fact or expert—as to the value, or a reasonable approximation thereof, of their alleged contributions to Astellas' '956 or '321 patents. Defendants admitted that they "have not performed any analysis, valuation, assessment or accounting of the monetary value of Defendants' contributions to the subject matter of the '321 patent." (Ex. MI, Resp. to Interrog. No. 35 at p. 10, Defs.' Resp. to Astellas' Third Set of Interrog.

(Signed by Drs. Xu and Wang on Oct. 14 & 15, 2019, despite Certificate of Service attesting to service "on October 11, 2019").)

426. Defendants further provided no other response to Astellas' interrogatory asking for the value of any of their alleged contributions to the '321 patent, so they should not be permitted to testify, as fact witnesses, to some previously known but undisclosed valuation of their alleged contributions. (*See* Ex. MI, Resp. to Interrog. No. 35 at p. 10, Defs.' Resp. to Astellas' Third Set of Interrog. (Signed by Drs. Xu and Wang on Oct. 14 & 15, 2019, despite Certificate of Service attesting to service "on October 11, 2019").)

427. Finally, the Court has already held that Drs. Wang and Xu are not permitted to testify as experts at all, specifically including any opinions as to the "significance" of their alleged contributions to Astellas' patents. (*See* 2020.06.09 Status Conf. Tr. at 14:5-15:3.)

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CERTIFICATE OF SERVICE

I hereby certify that this document, which was filed with the Court through the CM/ECF system, will be sent electronically to all registered participants as identified on the Notice of Electronic Filing, and paper copies will be sent on August 10, 2020 to those identified as non-registered participants.

/s/ *David P. Frazier*
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